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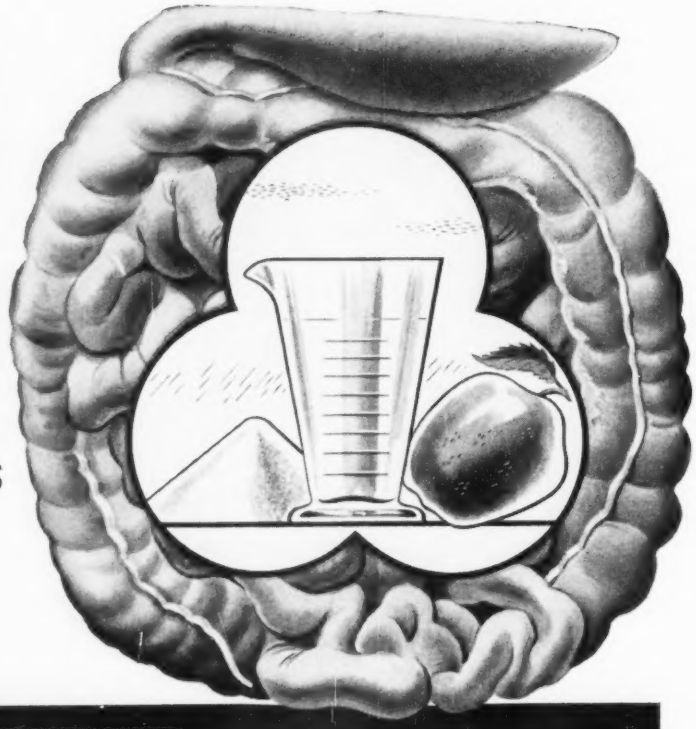

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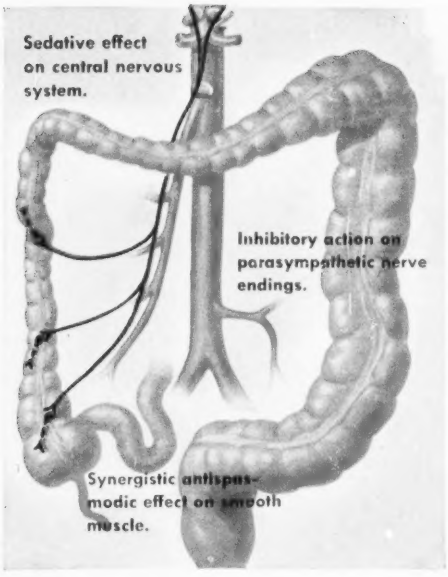
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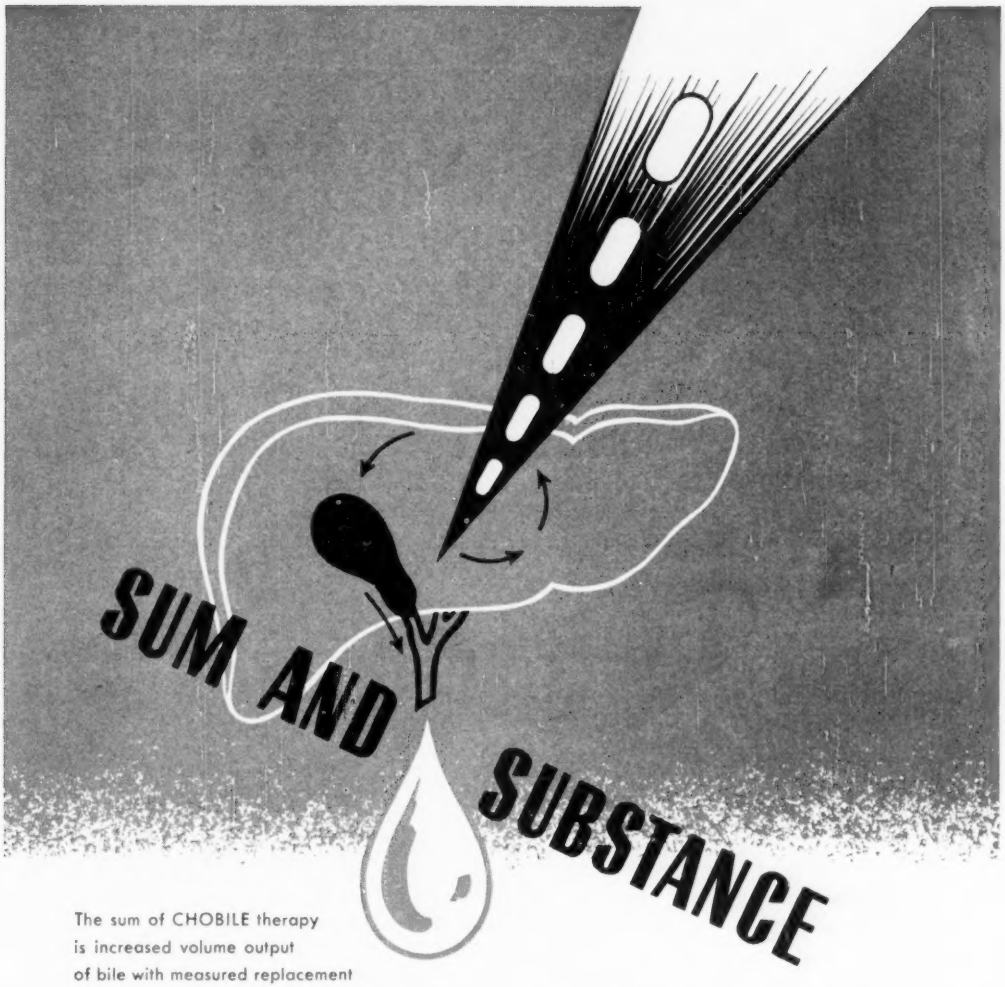

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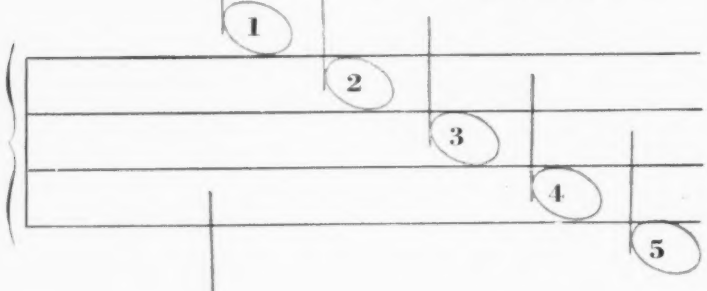

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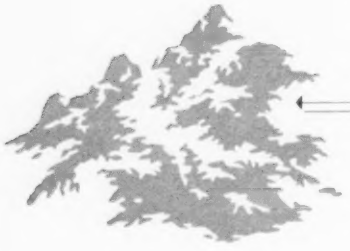

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PREDIABETICS: WHAT BECOMES OF THEM?

HENRY J. JOHN, M. D. Cleveland, Ohio.

THE TERM, *prediabetic*, is here used to designate any abnormal elevation of the blood sugar level, however slight, either fasting or before meals. In a strictly normal individual, the blood stream is cleared of excessive sugar before the following meal; in a prediabetic this is not always true. He will show a slight elevation of blood sugar before each meal or before one or two of them. From a practical standpoint, preprandial determinations of the blood sugar give essentially the same information as the glucose tolerance test. When the latter is used as the guide, the prediabetic is that individual whose blood sugar does not return to normal within three hours, but shortly thereafter, since in the normal individual, the normal level is reached within one to two hours.

Twenty-five years ago, when I was first confronted with patients of this type, I determined to follow as many as possible to find out what actually the final outcome would be in regard to the presence or absence of diabetes. Would they develop frank diabetes? Would the condition remain stationary? Or would the slight aberration in carbohydrate metabolism correct itself with time?

Since 1921, I have been able to follow fifty-five such patients for periods ranging from one to twenty-five years. Sixty per cent of these developed diabetes; in 40 per cent the condition remained stationary during the period of observation. The actual clinical course in thirty-one of these fifty-five cases is presented in the following reports and charts. As the data show, it is difficult to make generalizations regarding these cases, except that diabetes is more likely to develop than not, even with careful attention to diet, and that any impairment of carbohydrate metabolism can never be safely ignored.

CASE REPORTS

Case 1. (Fig. 1).—A man, 50, consulted me in 1921 after glycosuria was found in the course of an examination for life insurance. He also had hypertension and albuminuria. The fasting blood sugar at the first examination was 182 mg percent, and heavy glycosuria was present. A glucose tolerance test, performed two days later, showed a diabetic type of curve. The patient was placed on a strict diet and the blood sugar returned to normal and remained so for eight years. Then, in 1929, there was some elevation of the blood sugar, and a glucose tolerance test a year later revealed a definite diabetic curve, with blood sugar levels higher than at the initial examination. Insulin was administered for a few days, the blood sugar returned promptly to normal, and he managed well without additional insulin until his death, in 1944, at age 73, from coronary occlusion. This is an instance of mild diabetes which remained mild for twenty-three years.

Case 2. (Fig. 2).—A woman, 48, when first seen in 1921, had suffered from periodic attacks of gall stone colic for thirteen years. She was obese, but reported that she had lost 15 pounds recently. The glucose tolerance curve at that time was normal. Four year later, 1925, the glucose tolerance test was repeated, and then showed a frankly diabetic curve. Insulin was administered for four days, and subsequently repeated checks of the blood sugar yielded approximately normal values for a period of ten years. Then the attacks of cholecystitis increased in frequency and the blood sugar level rose concomitantly. The patient, however, refused to take insulin, because she felt, in view of her past experience, that the condition could be controlled by diet alone. The blood sugar remained high, and finally jaundice developed, and she was admitted to the hospital for treatment. Insulin was administered and the dosage increased during this illness, which involved a drainage of the gallbladder, followed by a pulmonary embolism. After about a month, the insulin could be discontinued, and the patient's blood sugar remained normal for two years. Then the blood sugar rose again and insulin had to be resumed. Shortly thereafter, a bundle branch block developed, and insulin was administered continuously except for a period of four weeks during the following year. The patient died in 1940, four years after the appearance of the heart difficulty, from coronary thrombosis, at age 67.

Cholecystitis frequently is a forerunner of diabetes. In this instance, however, a definite abnormality in glucose tolerance did not appear until seventeen years after the onset of gall bladder colic, and the patient did not become a frank diabetic until twenty-four years after the symptoms of cholecystitis were present. After this development, though, there was no reversal and she remained diabetic to the end of her life.

Case 3. (Fig. 3).—A man, 59, who consulted me in 1922 had been told two years previously that he had glycosuria when he was examined for life insurance. He had been placed on a restricted diet and the glycosuria had disappeared. At my first examination, the fasting blood sugar was just slightly elevated and there was a trace of sugar in the urine. A glucose tolerance test three days later showed a prediabetic type of curve, since the blood sugar the third hour was somewhat above normal. I placed him on a slightly restricted diet, and followed his progress, with periodic examinations. For seven years, the blood sugar (fasting) was elevated at times and at other times normal, and during this time he took insulin on two occasions for relatively short periods. On January 4, 1929, after insulin had been discontinued for eight months, a glucose tolerance curve was frankly diabetic. However, following this, he continued to show normal fasting blood sugar levels for a year, without taking insulin. Then insulin was reinstated. Two years later, in 1932, hyperthyroidism developed, and he died six days after thyroidectomy, of thyroid crisis, at age 69.

This case illustrates the gradual development of diabetes over a ten year period, which culminated with death at age 69 from hyperthyroidism.

Case 4. (Fig. 4).—In 1922, I examined a man, 45, apparently in good health in whom diabetes had recently been discovered. His father had died of diabetes. The first glucose tolerance test showed a frankly diabetic curve, but on restricted diet alone, his blood sugar remained relatively normal for ten years. In 1932, it was found that diet no longer controlled the condition, and insulin administration was begun in small doses. With the passage of the years, the insulin dosage had to be increased gradually, to keep the diabetes under control. The patient died at age 70 from general debility and cerebral arteriosclerosis.

This case showed the gradual decrease in sugar tolerance in a man who followed his dietary regimen carefully and thus managed to live his normal span of years.

Case 5. (Fig. 5).—When I first saw this patient, a man 31, he stated that diabetes had been discovered by another physician nine months earlier. Since that time he had been taking a restricted diet and had lost 20 pounds. At my first examination, on April 8, 1924, the blood sugar was 127 mg per cent and the urine contained a trace of sugar. During the ensuing three years, blood sugar determinations usually showed normal values. In January, 1928, the glucose tolerance test showed a diabetic curve, and the blood sugar became more difficult to control by means of diet. A year and a half later, in June, 1929, the patient began to take insulin and, except for a few short intervals, has continued taking insulin.

Figure 5 shows the course of progression of diabetes in this patient over an eight-year period. At first the diabetic condition was extremely mild but gradually increased in severity.

Case 6. (Fig. 6).—A man, 41, consulted me first in 1924, because glycosuria had been found when he had been ex-

amined for life insurance four months earlier. Since the initial finding, it had been present in some and absent in other urine examinations; and the patient had lost 34 pounds. One sister was also diabetic. My examination disclosed no glycosuria and the fasting blood sugar was 127 mg per cent. A glucose tolerance test a week later was normal. Twelve years later, in 1936 a glucose tolerance curve was frankly diabetic. The hyperglycemia was fairly well controlled for a time by means of diet, but in 1944, the patient had to begin taking insulin to control the condition.

This case furnishes another instance of relatively mild diabetes for a twenty-year period, which eventually became severe enough to require regular administration of insulin for its control.

Case 7. (*Fig. 7*).—When this patient, 40, consulted me in 1925, his history disclosed that he had had the classical symptoms of diabetes five months previously, and in the interim had lost 28 pounds in weight. When I examined him, he had no glycosuria, but the blood sugar was 147 mg percent four hours after a meal, and two days later, a glucose tolerance test showed a frankly diabetic curve. Insulin was administered for a few days, and the blood sugar level returned to normal. Tertiary syphilis was also discovered and the patient began an intensive course of treatment for this disease. Three years later, a glucose tolerance test showed a level of blood sugar much higher than on his initial examination. A year later, in 1929, the glucose tolerance test showed normal findings. The question naturally arises as to whether the grossly abnormal glucose tolerance shown in the second test was the result of hepatitis caused by the antiluetic treatment. This patient, an unscrupulous character, exploited the fact that his blood sugar had returned to normal by selling a patent antidiabetic device, called the Sanovapor, to diabetics throughout the state, and clinched his sales by showing his own clinical record of its efficacy.

Case 8 (*Fig. 8*).—A man, 61, had not been feeling well for several months and had been having fatty stools. He reported that sometime earlier another physician had advised him that he had glycosuria. He confessed to being a heavy eater. The fasting blood sugar, at his first visit, in 1926, was 147 mg per cent and there was no glycosuria. He returned to see me five years later and then a glucose tolerance test showed a diabetic curve. Subsequent fasting blood sugars, over a three-week period, were normal. A second glucose tolerance test a month later was approximately the same as the first determination.

This patient presents an example of a mild or potential diabetic in whom impaired sugar tolerance is demonstrated only by a heavy load of carbohydrate. I should venture the prediction that if he had been followed for another ten years, the development of frank diabetes would have been evident.

Case 9 (*Fig. 9*).—A boy 10, developed classical symptoms of diabetes, with some loss of weight and heavy glycosuria, following a fever of unknown origin. He was referred to me by the family physician and my first examination, in 1926, showed a blood sugar of 270 mg percent, with severe glycosuria. Insulin was administered immediately and the blood sugar returned to normal. After treatment for sixteen days, it was possible to discontinue the administration of insulin, and the blood sugar remained normal for three months, merely on a restricted diet. Then the patient had a cold, and the blood sugar increased, and insulin had to be reinstated in higher doses. This was discontinued after a month, and the blood sugar remained normal for a time. Five months later, administration of insulin had to be resumed, but small doses sufficed for reasonable control of the blood sugar. Then his parents decided that they would take him to Kansas City, where they had been promised his diabetes would be cured by placing him in the oxygen tank. He did not return to my care, but I received a report that he died in 1943, i.e., seventeen years after onset of his diabetes, from a kidney affection. I suspect that this was intercapillary glomerulosclerosis.

Case 10 (*Fig. 10*).—A man, 21, consulted me in 1926 because glycosuria had been discovered on a routine physical examination. He had no symptoms and no complaints. As soon as the glycosuria was discovered, he had begun restricting his diet,

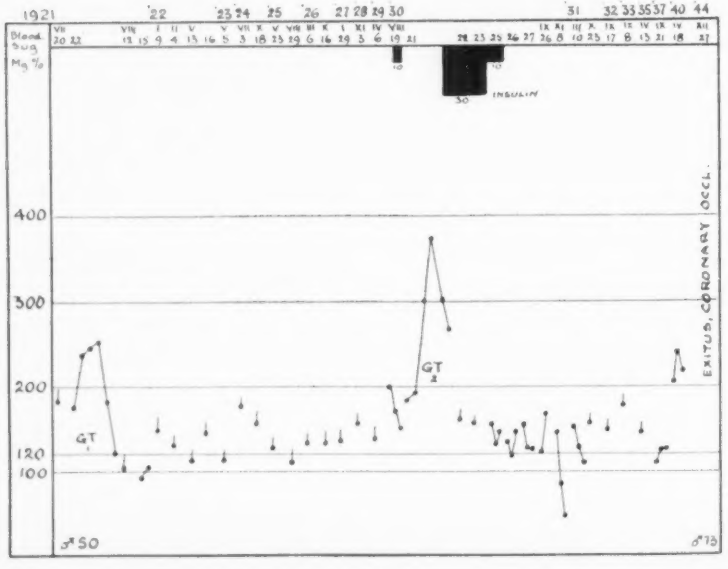
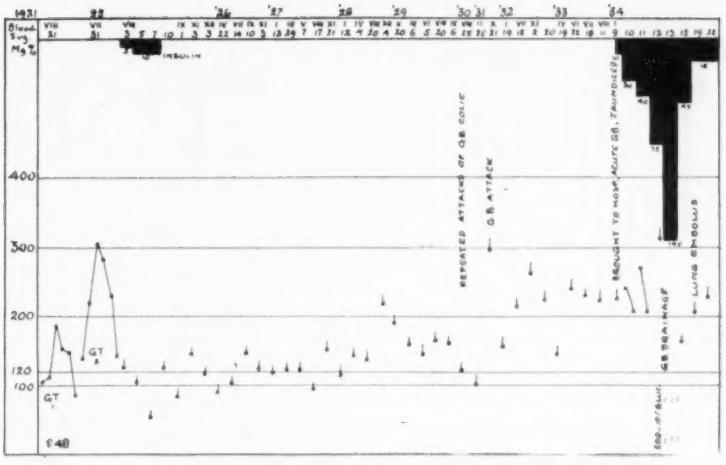


Fig. 1. Case 1.



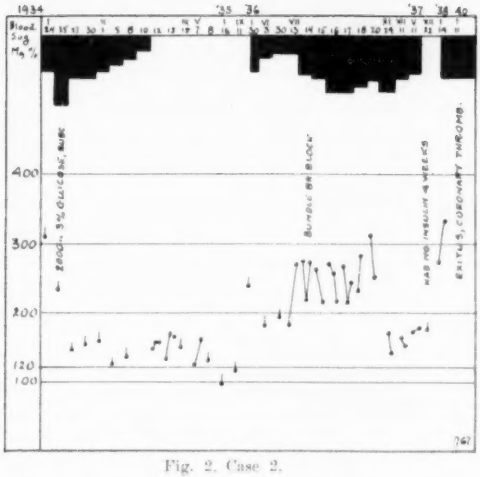


Fig. 2. Case 2.

although he had never been overweight, because he had a great fear of diabetes. There was no history of the disease in his family, however. The first blood sugar determination, taken two and a half hours after eating, was normal, i.e. 82 mg per cent. A glucose tolerance test on the following day showed a prediabetic type of curve. Several fasting blood sugar determinations made in 1927 were normal. The following year, 1928, the glucose tolerance curve was still of the prediabetic type. Glucose tolerance tests in 1930 and 1931 showed a little lower levels of the blood sugar. Fifteen years later, in 1946, after disregarding dietary restrictions, the glucose tolerance test showed a diabetic curve. A year later the situation was improved, although the glucose tolerance test showed some impairment in sugar metabolism (prediabetic curve). A check six months later revealed that the blood sugar was normal in the morning (fasting) and before lunch, but that two hours after lunch it was slightly elevated.

In this case, this prediabetic patient has remained so for twenty-one years, because with a single exception, he has adhered rigidly to a restricted diet, and has kept himself consistently under weight. In 1926, when I first saw him, his weight was 125 pounds (-22 per cent). In 1930 it was 144 pounds (-9 per cent; in 1931, 140 pounds (-11 per cent) and in 1947, 123 pounds (-22 per cent). His careful attention to his diet probably accounts for the fact that frank diabetes has never developed; apparent evidence on this point is that the one significant increase in blood sugar during this long period occurred following a lapse in this dietary regulation.

Case 11 (Fig. 11).—A man, 50, consulted me in 1926 because glycosuria had been found in an examination for life insurance. The patient was in excellent health, but reported that his father and two brothers had died of diabetes. The first blood sugar determination, two and a half hours after a meal showed a level of 219 mg per cent, and glycosuria was pronounced. After administration of insulin for a few days and a restricted diet, the blood sugar returned to normal, and over a period of thirteen years, the condition was fairly well controlled on diet alone, with occasional short periods of insulin administration. Since October, 1939, however, insulin has been required constantly and in increasing doses.

This case illustrates satisfactory control through insulin, in a patient who prefers not to restrict his diet too rigidly. Now, at age 71, he is in good health, although frankly diabetic, twenty-one years after a mild impairment of sugar metabolism was discovered. He died in Dec. '49 of coronary occlusion.

Case 12 (Fig. 12).—A man, 46, consulted me in 1927 because glycosuria had been found in the course of a physical examination for life insurance. The first glucose tolerance test showed only the slightest lag in carbohydrate metabolism, since it required a little over two hours for the blood sugar to drop to 120 mg per cent. When the glucose tolerance test was repeated four years later, in 1931, the lag had increased, since the blood sugar did not return to normal for two and three-quarters hours. A year later in 1932, there was still

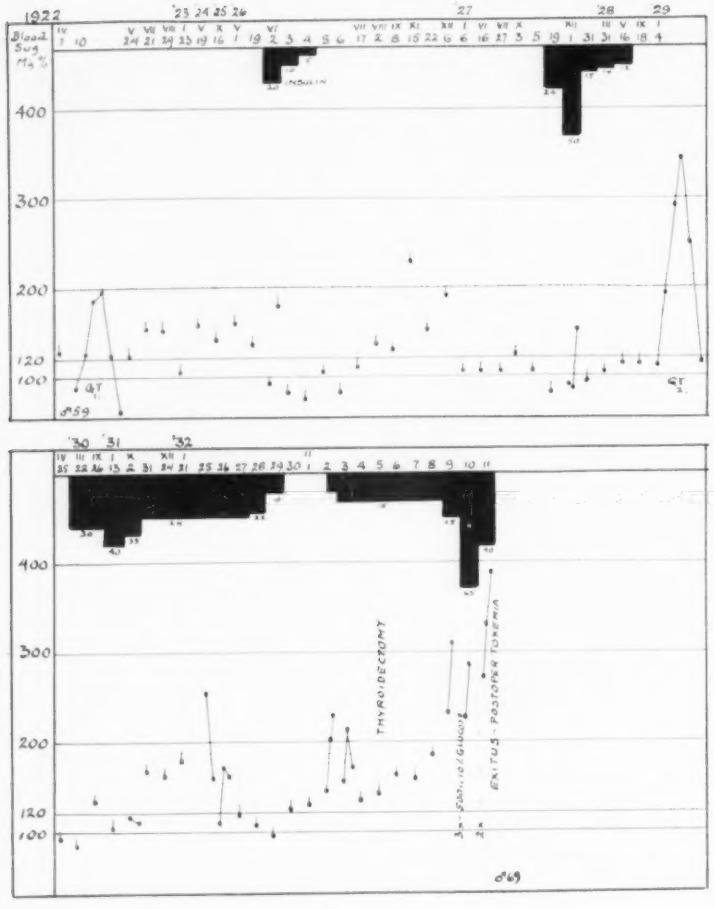


Fig. 3. Case 3.

further decrease in sugar tolerance. In December, 1932, three blood sugar determinations, made before meals, were normal. The patient had been taking practically a normal diet, but avoiding pastries and overeating. In 1936, the glucose tolerance curve showed increasing abnormality, and even the fasting blood sugar was slightly above normal. In 1938, the three blood sugar determinations, before meals, became definitely elevated; the same year, the patient suffered an attack of angina at which time the fasting blood sugar level was quite high. In 1939, the glucose tolerance test showed a high curve, which started above 200 mg percent and was almost 300 mg per cent at the end of the fourth hour. The patient then had to take insulin which was increased to 50 units per day to effect reasonable control of the diabetic condition. On November 19, 1939 he had a coronary thrombosis and five months later, in April, 1940, jaundice with fever. After this episode it was possible to reduce the insulin dosage and still maintain a satisfactory glycemic level. Insulin was even discontinued for a short time, in 1941, but had to be reinstated. The patient died in June, 1942 of coronary occlusion.

This case, followed for fifteen years, furnishes a good illustration of the gradual development of diabetes, in a man past middle age, who was very cooperative and exercised moderation and care in his diet. In this instance, the deviation of the blood sugar curve at the outset was very slight indeed, but the deviation from normal became more and more apparent and finally culminated in frank diabetes which had to be treated continuously with insulin and dietary restriction.

Case 13 (Fig. 13).—A youth, 17, consulted me in 1927 and stated that diabetes had been discovered four months earlier, at which time he had classical symptoms of the disease, with a blood sugar of 286 mg per cent. He had been sent to the hospital for four days and took insulin for ten days at that time. He had lost 19 pounds in weight. His maternal grand-

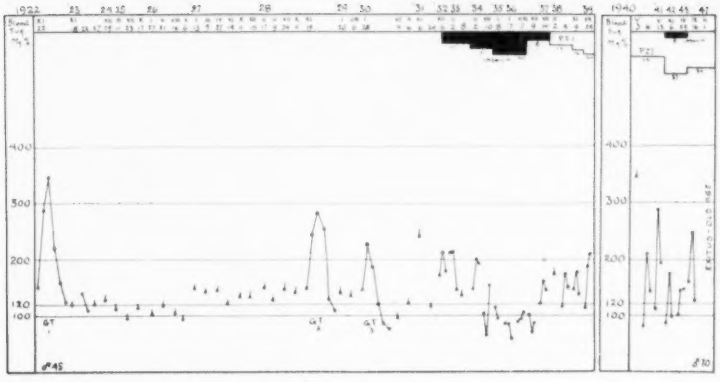


Fig. 4. Case 4.

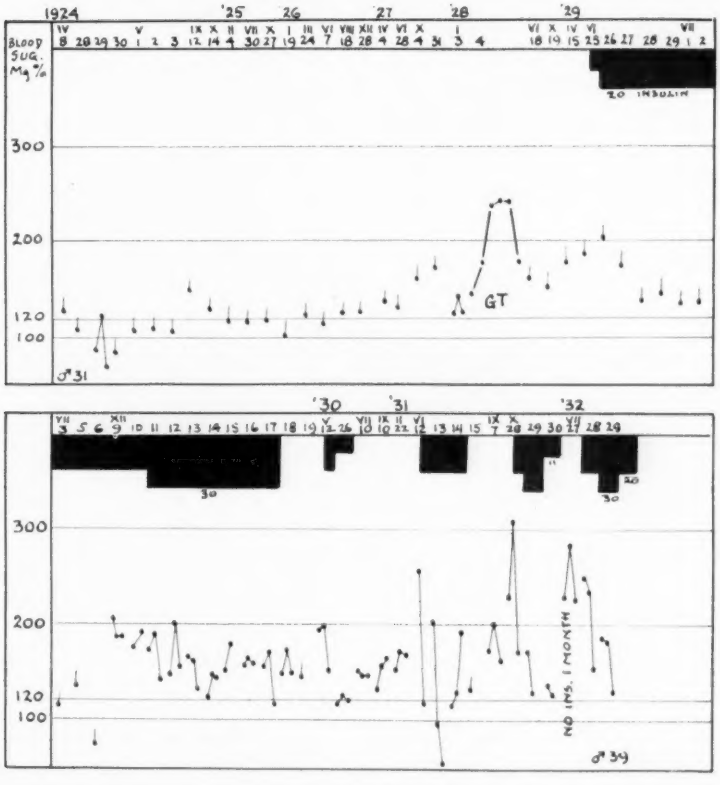


Fig. 5. Case 5.

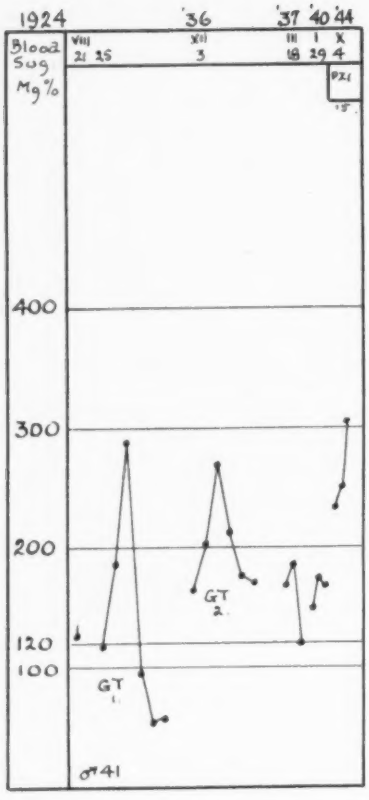


Fig. 6. Case 6.

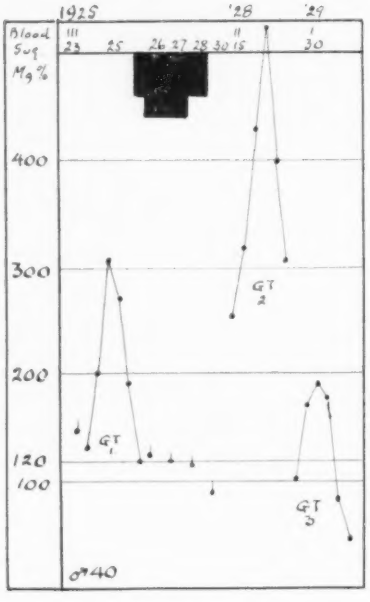


Fig. 7. Case 7.

father had diabetes. At my first examination, all three preprandial blood sugar determinations were normal and there was no glycosuria. The blood sugar three months later was 100 mg per cent. However, a glucose tolerance test on the following day showed a diabetic curve. A second glucose tolerance test, performed eight months later, showed somewhat lower values, but the curve was still of diabetic type. The fasting blood sugar in January, 1929, was normal. In October of the same year, blood sugar values were elevated, and the glucose tolerance curve was frankly diabetic. Insulin was administered for a few days, and repeated blood sugar determinations thereafter yielded normal values. In April, 1930, the glucose tolerance curve was again frankly diabetic. Adherence to a strict diet at that time reduced the blood sugar, but about a year later, it rose considerably. The patient was placed on insulin, on which he has continued, without interruption.

This case represents an instance in which diabetes developed at age 17, as indicated by classic symptoms and a high blood sugar level. Apparently, however, considerable insulinogenic reserve remained, and the pancreas resumed fairly normal function for a considerable period, but eventually the reserve was exhausted, and frank diabetes recurred, and continued.

Case 14 (Fig. 14).—An overweight woman, 54, stated at her first examination in 1927 that glycosuria had been discovered a year earlier and had been present intermittently since. Her fasting blood sugar was 174 mg per cent. Nearly a year later the glucose tolerance curve was frankly diabetic. A small dosage of insulin was given for a few days and this brought the blood sugar to a level satisfactory for her age. Afterwards, control was satisfactory, with diet alone. I followed her progress for four years, until 1931, and a letter from her in 1946 stated that she had remained in good health on a slightly reduced diet.

Case 15 (Fig. 15).—A woman, 51, was first seen in 1929 because of the discovery of glycosuria. The fasting blood sugar was 130 mg per cent with slight glycosuria. A week or so later, the glucose tolerance curve was diabetic. A slight restriction in diet was prescribed, and for the following three years, the blood sugar remained at a normal level. No insulin was used at any time.

Case 16 (Fig. 16).—A man, 58, had known of the presence of diabetes for a year when I first saw him in 1931. A diagnosis of syphilis had been made six years earlier, in 1925, but

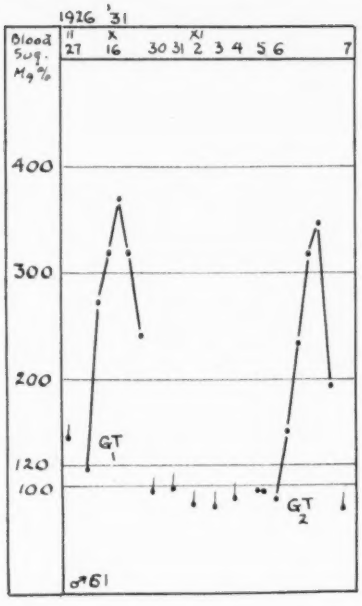


Fig. 8. Case 8.

he had had no adequate treatment for this until a short time before he consulted me. Two weeks earlier, he had had intense jaundice, which had cleared somewhat by the time I examined him. The fasting blood sugar on March 2, 1931 was 119 mg per cent, and a glucose tolerance test the following day showed a diabetic curve, with the fasting blood sugar 148 mg per cent. It appeared possible and likely that the elevation of the blood sugar level was due to the hepatitis, especially since subsequent checks of the blood sugar were normal for several years. Finally, however, there was some elevation of the blood sugar, though this was not severe until 1945, fourteen years after my first examination. Then insulin was given for about a year, but for the past three years his condition has been satisfactory without continuous administration of insulin. At age 74 this patient is well and extremely active, and his appearance is that of a man of 60 years.

Case 17 (*Fig. 17*).—In 1931, a man, 45, consulted me because of the findings of glycosuria. He was not overweight, had no complaints and there was no history of diabetes in his family. A glucose tolerance curve was frankly diabetic, and subsequent checks of the blood sugar over a period of thirteen years showed increasing elevation of the blood sugar, which finally, in 1944, required the administration of insulin. With continuous administration of insulin, the diabetes has remained in fairly good control.

This case is another instance in which is seen the gradual development of diabetes over a period of years, despite satisfactory attention to diet and the absence of apparent precipitating factors.

Case 18 (*Fig. 18*).—On original examination of a woman, 58, in 1931, there was but slight elevation of the blood sugar levels. Afterwards, the blood sugar showed some increase, but this was not of pronounced degree. In August, 1932, insulin was administered for five days; this reduced the blood sugar promptly and no more insulin was required for two years. An appendectomy was performed during this period. In January, 1935, the blood sugar increased and insulin, in increasing dosage, had to be administered for some time before the hyperglycemia was brought under satisfactory control. Then the dosage was reduced somewhat, but its administration had to be continued. The patient had a streptococcic infection of the throat, in 1937, and died of septicemia resulting from this at age 64. Necropsy revealed the presence of portal cirrhosis of the liver.

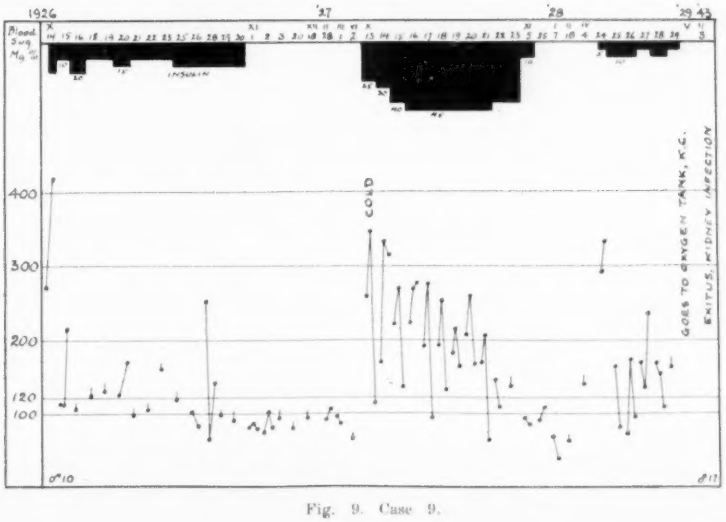


Fig. 9. Case 9.

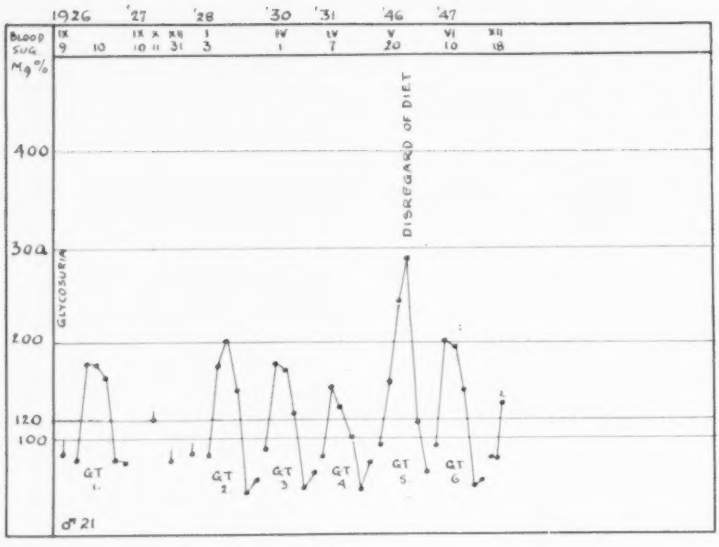


Fig. 10, Case 19.

In this instance, a relatively mild diabetic condition progressed within six years to a severe diabetes, brought to crisis and exitus by a severe infection.

Case 19 (Fig. 19).—A man 46, presented himself for examination because of a finding of glycosuria, in 1933. The initial fasting blood sugar was 186 mg per cent. On the following day, the fasting blood sugar was normal but the glucose tolerance curve was of diabetic type. Subsequent checks of the blood sugar during the following year showed but slight elevation. A glucose tolerance test, performed two years after the first one, showed a similar curve, but subsequent checks of the blood sugar were normal. The patient's condition remained mild throughout an eight year period. Then, in 1941, the patient died at age 54 from coronary occlusion.

Case 20 (Fig. 20).—A woman, 46, was seen first in 1933 because of a recent finding of glycosuria. She was a very active woman socially and was very fond of sweets and candy. At examination, she had a heavy glycosuria and the blood sugar one hour after eating was 263 mg per cent. This frightened her and she followed a restricted diet carefully for several years, during which time the blood sugar was in reasonable control. In time, however, she became careless and five years afterward, the blood sugar levels increased markedly. In December, 1938, the administration of insulin was instituted. During the next seven years, there were times when the blood sugar was considerably elevated as the result of overeating of candy, but from 1943 onward, control of hyperglycemia was adequate on steadily decreased amounts of insulin. Hypertension had been present from the outset and in June, 1946, she had a cerebral hemorrhage. The patient is still living.

In this case, with time, there was a progression of diabetes and then a retrogression. The latter may have been due to a decrease in food intake.

Case 21 (Fig. 21).—A man, 42, had had diabetes for one year when I examined him in 1933. At that time, the fasting blood sugar was normal and there was no glycosuria, yet a glucose tolerance curve made two days later was frankly diabetic. A restricted diet was prescribed and subsequent checks showed a normal blood sugar level for seven years, until 1940, when my observation of the patient ceased.

This is an instance in which a mild diabetic condition remained mild, with only slight dietary restriction.

Case 22 (Fig. 22).—When this man was first seen in June, 1933, at age 64, he stated that glycosuria had been found a few months previously. He had had frequent examinations of the urine for years previously and it had never been present. His two brothers were diabetic and later his son became afflicted with the disease. The first blood sugar determination showed an increased level, 247 mg per cent. On a restricted diet, hyperglycemia was brought under control and the blood sugar remained normal for three years. In 1936, however, it began to rise and administration of insulin was begun in 1937. Attempts were made to discontinue insulin from time to time, but it always had to be resumed. The patient died in 1940, seven years after I first saw him of coronary occlusion.

This is another instance in which the diabetes remained mild over a period of years, but eventually progressed to the point where insulin was required for its control.

Case 23 (Fig. 23).—A girl, 13, was brought to me in 1934 because glycosuria had been discovered four days earlier. She had had vulvar itching for six weeks, but was otherwise in good health. There was no history of diabetes in the family, and the child was not overweight. A glucose tolerance test showed a diabetic type of curve. With dietary restriction, however, subsequent blood sugar levels were normal for the next nine months. Then a glucose tolerance test showed a normal curve. Her progress was satisfactory for several years. Then she married, and had a miscarriage, and after this the blood sugar increased to a high level and large dosages of insulin were required to bring her under control. She continued to take insulin and remained in apparent good health, but hemorrhagic retinitis developed, which caused her to lose her sight, in 1948, fourteen years after the onset of diabetes.

This case is that of mild diabetes in a young person, easily controlled by diet, which culminated in a complete upset of

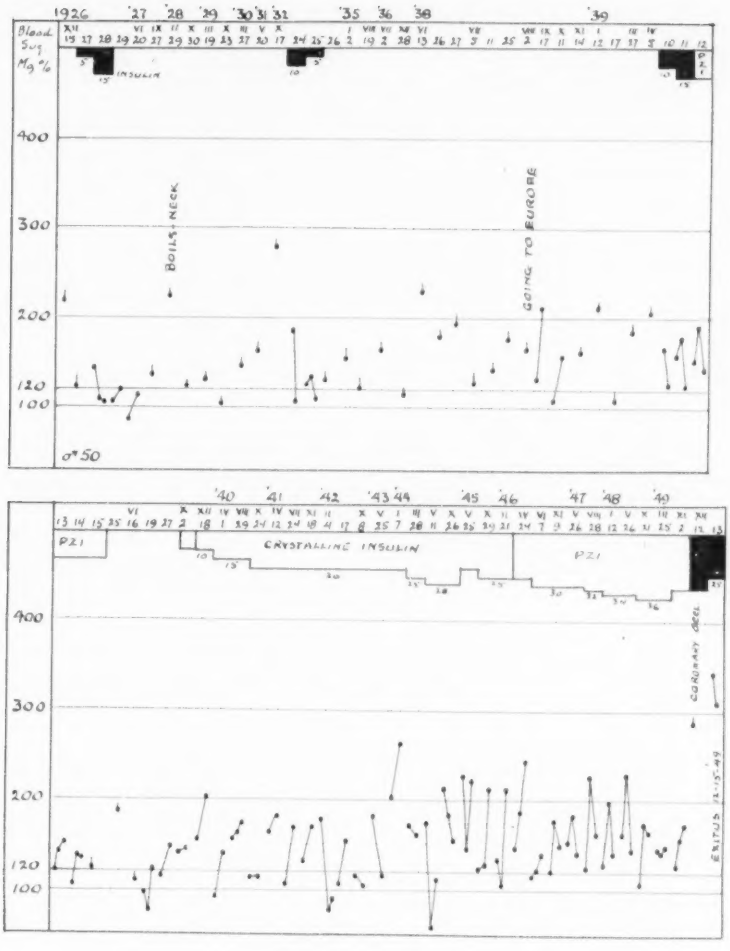


Fig. 11. Case 11.

carbohydrate metabolism after a miscarriage, with the development of ocular symptoms which eventually resulted in blindness.

Case 24 (Fig. 24).—An obese man, 49, gave a history of the discovery of glycosuria two years before I saw him in 1936. This finding had disappeared in the meantime. There was no history of diabetes in the family. The first blood sugar determination was only slightly above normal. Subsequent checks demonstrated progressive elevation of the blood sugar level, until 1944, when insulin had to be given. He has continued to take insulin, but the control has not been entirely satisfactory, owing to dietary indiscretion.

This case furnishes another example that even the slightest elevation of blood sugar cannot be ignored, since it is likely in later years to progress to frank diabetes.

Case 25 (Fig. 25).—When first examined in 1938, this man was aged 38 years. He had then been receiving treatment for diabetes for two years and had been following a strict diet. When I first saw him, he was overweight and his blood sugar at 5 P. M. was 164 mg per cent, with a pronounced glycosuria. He continued on dietary treatment for a few months but in October, 1936, administration of insulin was begun and has had to be continued ever since. At times, there was considerable elevation of the blood sugar, especially during the war the diabetic condition has remained in fairly satisfactory years, when he was under heavy strain. Recently, however, control.

This case shows the steady progression of diabetes over a

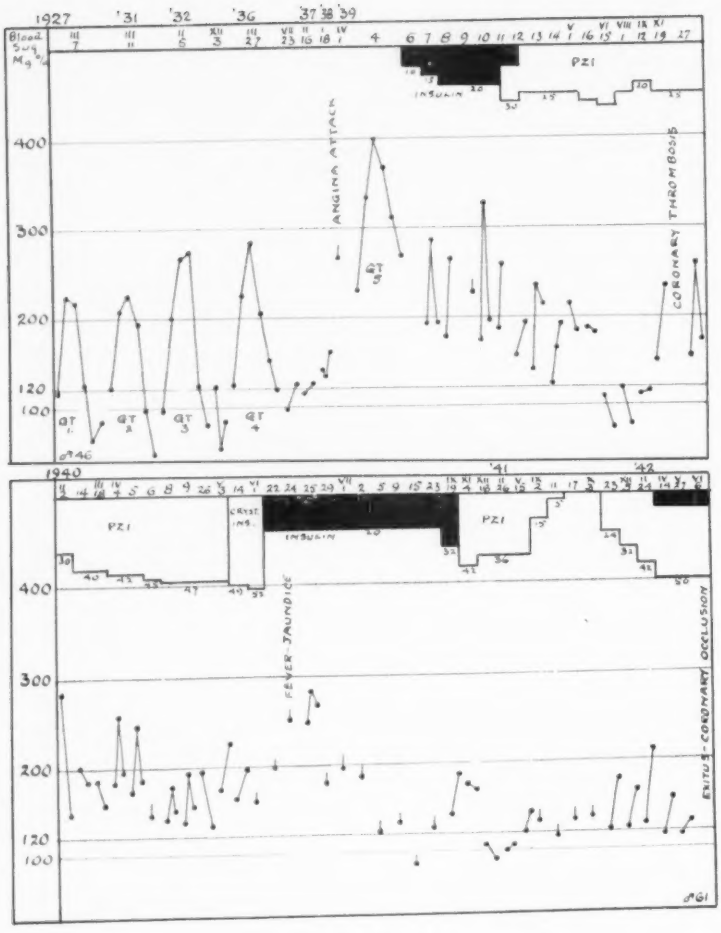


Fig. 12. Case 12.

twelve year period in a man who is intelligent and cooperative and quite careful in following his dietary regimen.

Case 26 (Fig. 26).—A man, 46, whom I saw first in 1937, had been told five years previously, and again five weeks earlier that he had glycosuria. The glucose tolerance curve was diabetic. After ten days of insulin administration, the blood sugar returned to normal levels. He has continued, with a regular diet, without further administration of insulin, and checks at intervals over a five year period, showed no further progression in the diabetic condition.

Case 27 (Fig. 27).—A man, 43, consulted me in 1938, because of glycosuria which had been discovered a year earlier. A glucose tolerance test showed an abnormal curve, so administration of insulin was carried out for two months, during which time the blood sugar returned to normal, and the patient lost some excess weight. The blood sugar remained normal, with no further insulin, for three years, when it began to rise, and since then, he has had to be on small doses of insulin at intervals from time to time, to keep the blood sugar level in good control.

This case shows the gradual evolution of diabetes in a business man of the high-pressure type, although it has remained relatively mild throughout a period of eleven years.

Case 28 (Fig. 28).—In 1939, a woman, 52, presented herself with complaints of thirst and loss of weight. At examination the preprandial blood sugar levels were 125, 196 and 254 mg per cent, and the urine contained considerable sugar. For seven years, she followed a 1700-calorie diet, and her blood

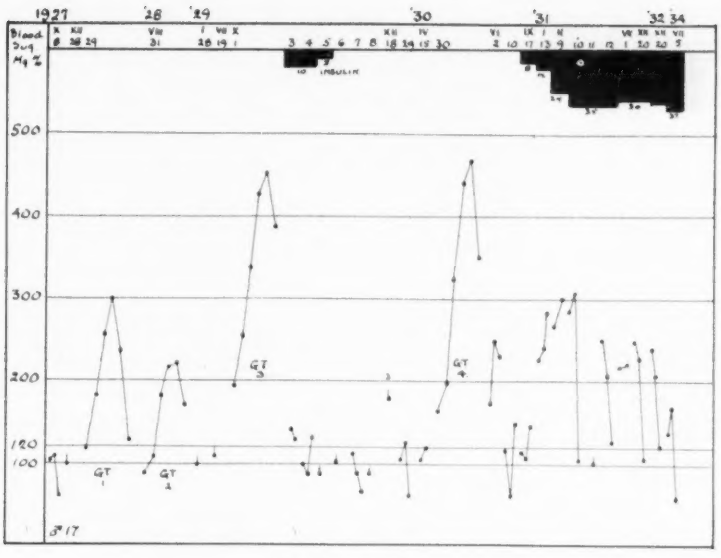


Fig. 13. Case 13.

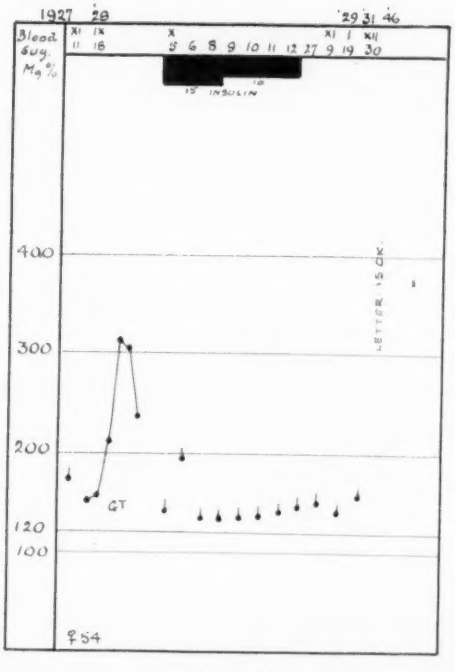


Fig. 14. Case 14.

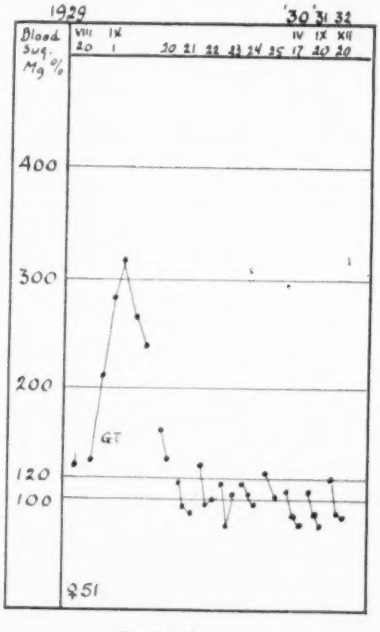


Fig. 15. Case 15.

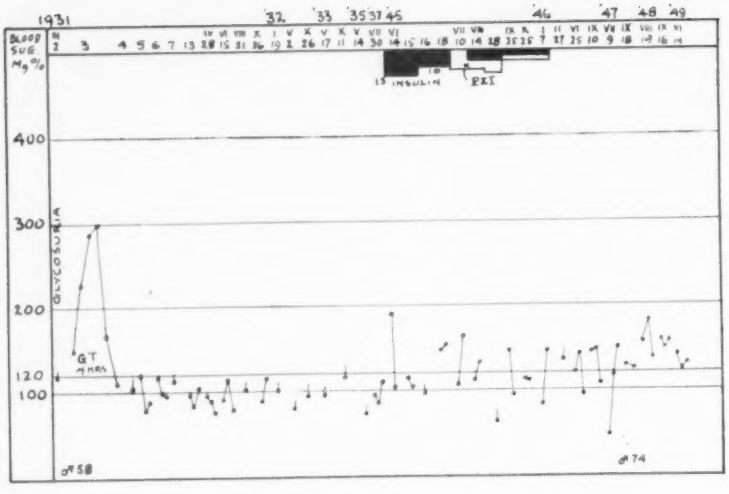


Fig. 16. Case 16.

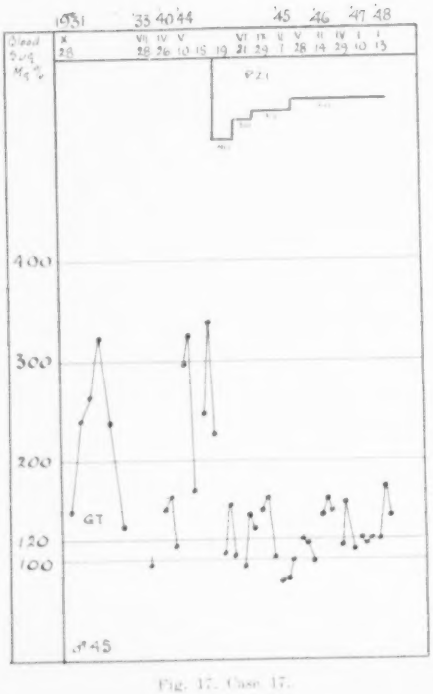


Fig. 17. Case 17.

sugar remained at or near the normal. In 1936, the blood sugar became elevated and insulin was necessary to control the diabetic condition. At age 62, she is in good health and travels a great deal, but her diabetic condition, despite control with diet and insulin, has progressed steadily during the ten years she has been under my observation.

Case 29 (*Fig. 17*).—A man, 55, presented himself for examination in 1939, because of a recent finding of glycosuria on routine physical examination. He had had urine examinations routinely for years, so knew that this was the first appearance of glycosuria. He was slightly overweight; there was no history of diabetes in his family. The blood sugar on the morning following the finding of glycosuria was 135 mg per cent, and all three preprandial blood sugar levels were elevated. He had always been a heavy candy eater and drinker of milk. He was told to omit these from his diet and to eat more moderately. The results were reflected immediately, for checks of the blood sugar during the following two months showed normal values. The glucose tolerance test three months after admission was normal. Everything progressed satisfactorily for two years. Then he had a severe respiratory infection and the blood sugar level was elevated to more than 300 mg per cent. After administration of insulin for three days, the blood sugar returned to normal. No further elevation occurred until three years later, in 1944, following a dental infection. Daily doses of 15 units of protamine zinc insulin for a month brought the condition under control. After 1946, he had occasional lapses into his old habit of candy eating, always with a corresponding elevation of the blood sugar.

The ten year observation in this case indicates that this patient, at the onset, had only a slight insulinogenic weakness, which probably was due to strain imposed by excessive eating of candy and milk drinking. He is nervous and energetic, the typical hyperkinetic individual, who is a business executive. Probably the diabetic condition has remained mild, despite his lapses of dietary control, because it was not due originally to any basic organic weakness of insulinogenic function, but rather to physiologic strain imposed upon it. Hence the diabetic symptoms appeared late, at age 55, and at that age, diabetes is likely to be mild, with any reasonable care. Such difficulties as this patient, at age 65, experiences, are due to

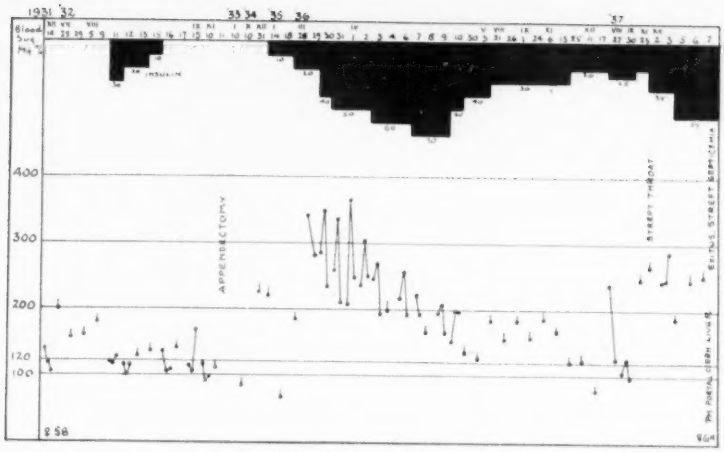


Fig. 18. Case 18.

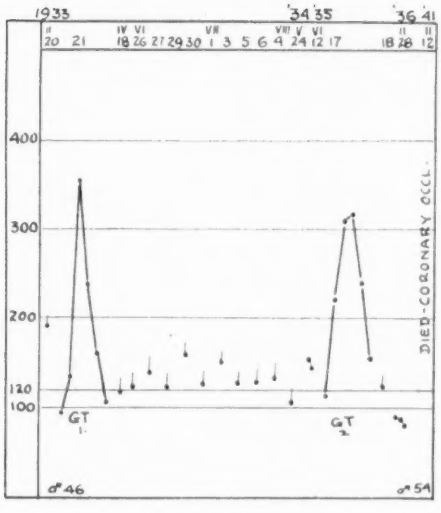


Fig. 19. Case 19.

his own violations of the prescribed regimen. When he behaves and cooperates, all is well.

Case 30 (*Fig. 30*).—A man, 46, who presented himself in 1940, stated that glycosuria had been found in the course of a life insurance examination three years earlier and that it had been present off and on since then. My first examination showed some elevation of the blood sugar level, but I was unable to convince him that he should take insulin until eight years later. Since the administration of insulin was begun, in 1948, the diabetic condition has remained in good control.

Although this patient followed a rigidly restricted diet for eight years, the mild diabetic condition progressed continuously and could not be brought under control until insulin was given.

Case 31 (*Fig. 31*).—A woman, 59, had been told recently that sugar was present in the urine. She was much overweight and had suffered from attacks of gallbladder colic periodically for years, but otherwise was in good health. There was no history of diabetes in her family. My first examination, in November, 1934, showed that the level of the blood sugar before all three meals was elevated, 234, 230 and 220 mg per cent. After administration of insulin for one week, the blood sugar returned to normal, and continued so for four years and nine months, on dietary control. Then she took a trip to Mexico and contracted a severe influenza; on her return, the blood sugar level had increased. Then insulin was administered in large doses for two months and the blood sugar returned to normal again and remained this way for fourteen months. Again an influenzal attack upset this control and insulin had to be reinstated and continued, with the exception of one very short interval, to the end of her life, in 1946, following a coronary occlusion.

Despite the fact that this patient was obese and had gall stones, two factors influencing the development of diabetes, the disease did not appear until age 59 and then remained relatively mild, with long recessions, only to progress markedly under the influence of infection. Dietary control in this case was not of the strictest, since the patient was obese, and "just loved candy and cake."

Discussion

The foregoing cases illustrate in a concrete way what actually happens in the course of the years in individuals who show a slight abnormality of carbohydrate metabolism. There has been some question among clinicians whether such a finding is of significance. As the records in this report demonstrate, this question can be an-

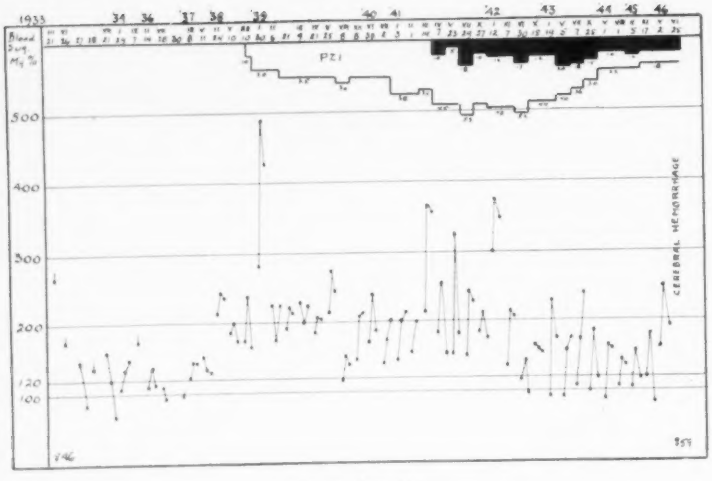


Fig. 20. Case 20.

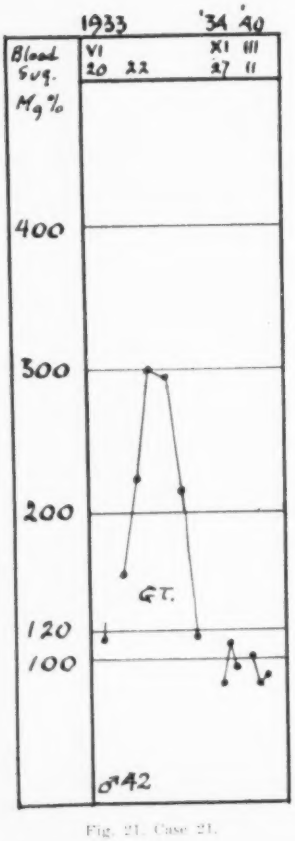


Fig. 21. Case 21.

swered in the individual case, only after years of observation. Observations for short periods are likely to be misleading.

In the series of fifty-five cases included in this presentation, followed for one to twenty-five years, frank diabetes eventually developed in thirty-three, or 60 percent, and twenty-two, or 40 per cent, did not show any significant progession of the prediabetic or potentially diabetic condition. The summary of these cases, showing the age at which the first indication of impaired glucose tolerance occurred and the length of time until diabetes developed or the length of time the patients were followed without developing diabetes, is shown in Figure 32.

Although, in general, this study shows that any impairment of carbohydrate metabolism, however slight, cannot be disregarded, since at least 60 per cent of such persons eventually have frank diabetes, it also demonstrates that no accurate prediction can be made in the individual case as to when or even whether diabetes will develop. With adequate dietary restriction, many of these patients continue without progressive impairment of insulinogenic function. In others, the condition is gradually progressive, despite adequate restriction of diet; and in a few, the condition remains stationary, despite dietary indiscretions. The unfavorable influence of infections, of pregnancy, liver disease, obesity, arterial degeneration and hyperthyroidism, in precipitating a change from mild to severe diabetes, or in increasing the severity of an already present diabetes, is well illustrated in this series of case histories.

Fluctuations in the diabetic state always constitute a problem in the clinical management of these patients. At times, a patient who has been taking insulin can omit it for long periods, with the blood sugar remaining at or near normal levels; and then, sometimes because of some intercurrent infection or other illness, dietary indiscretion, or for no apparent reason, the blood sugar is again elevated and requires reinstatement of insulin for its control. For this reason, patients

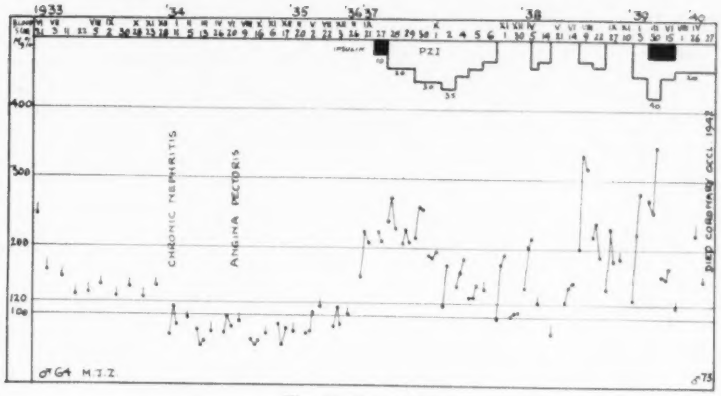


Fig. 22. Case 22.

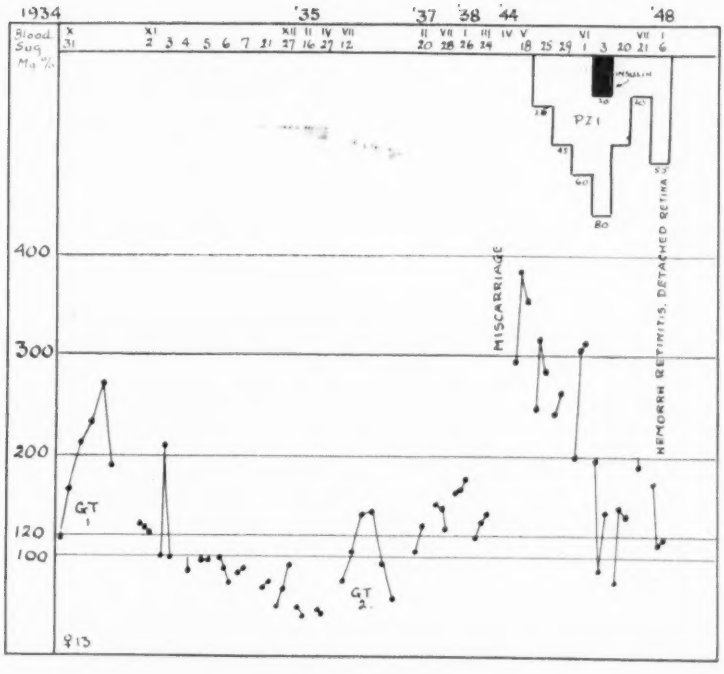


Fig. 23. Case 23.

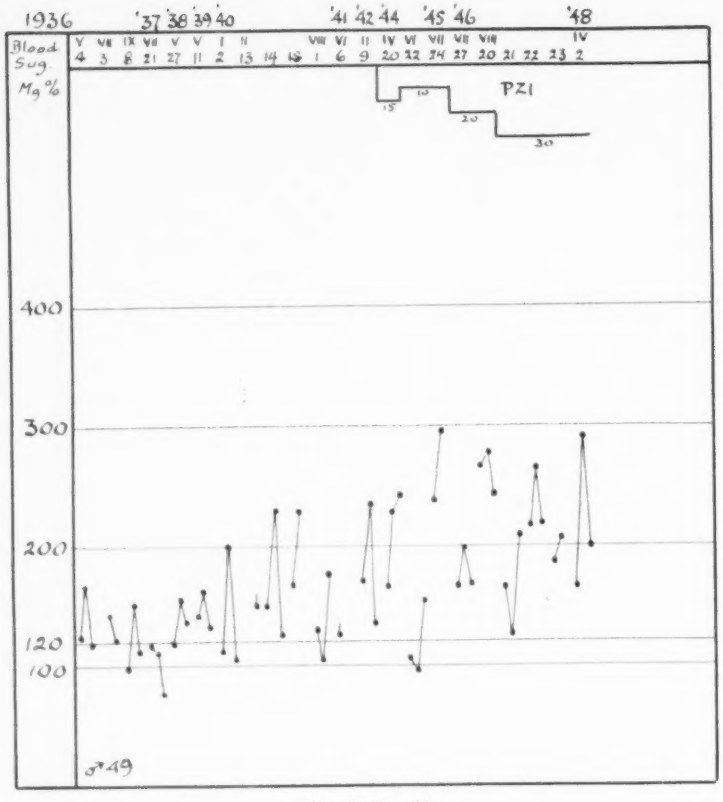


Fig. 24. Case 24.

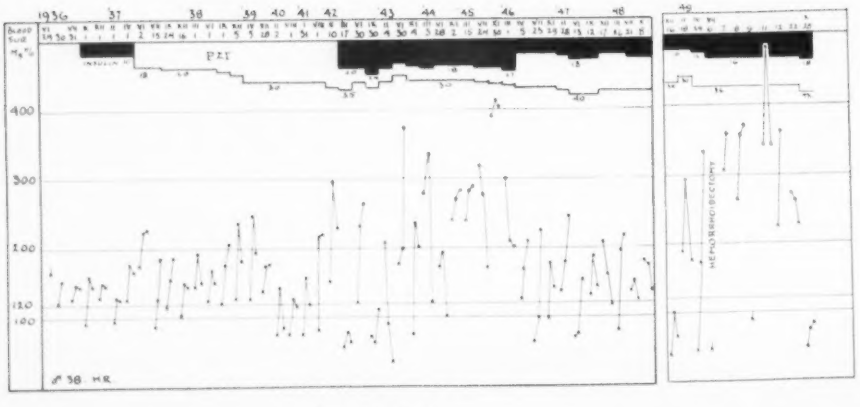
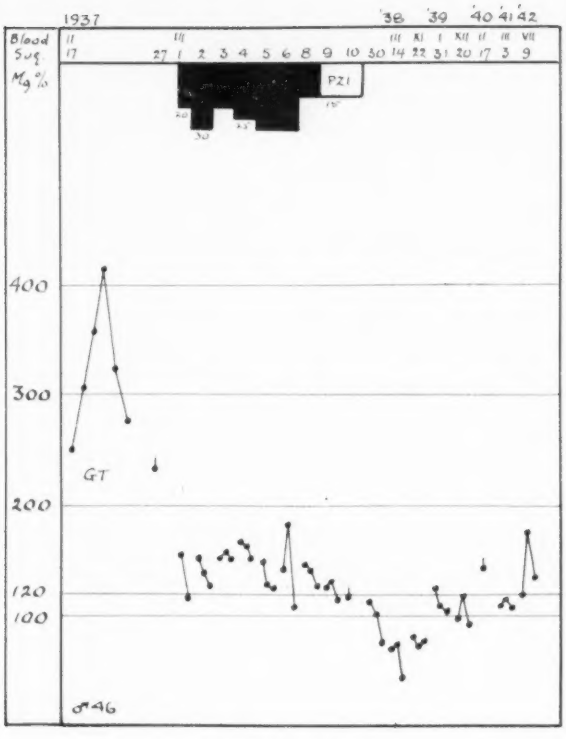


Fig. 25. Case 25.



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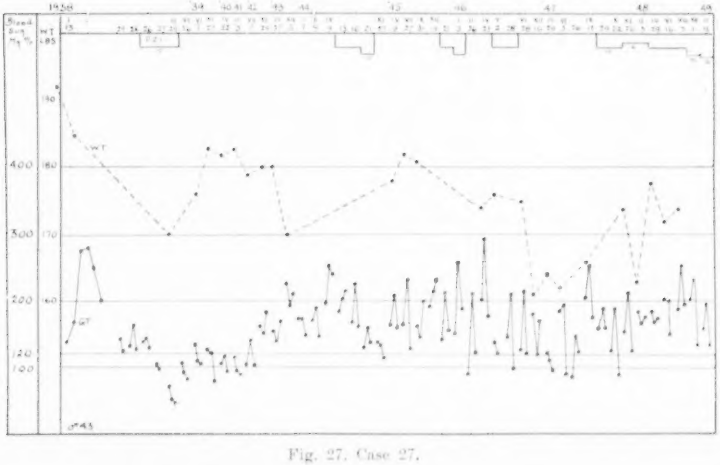

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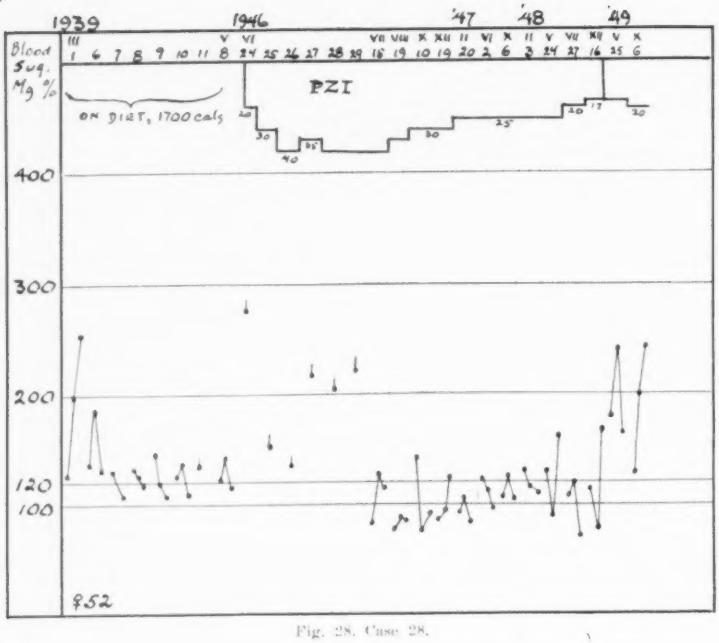

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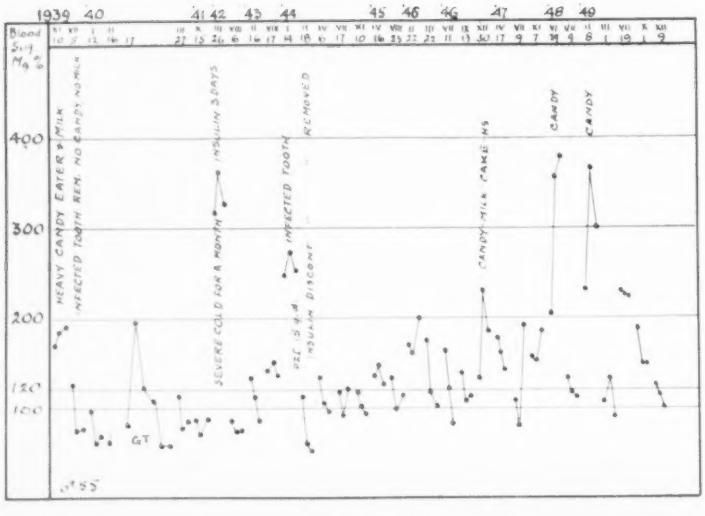

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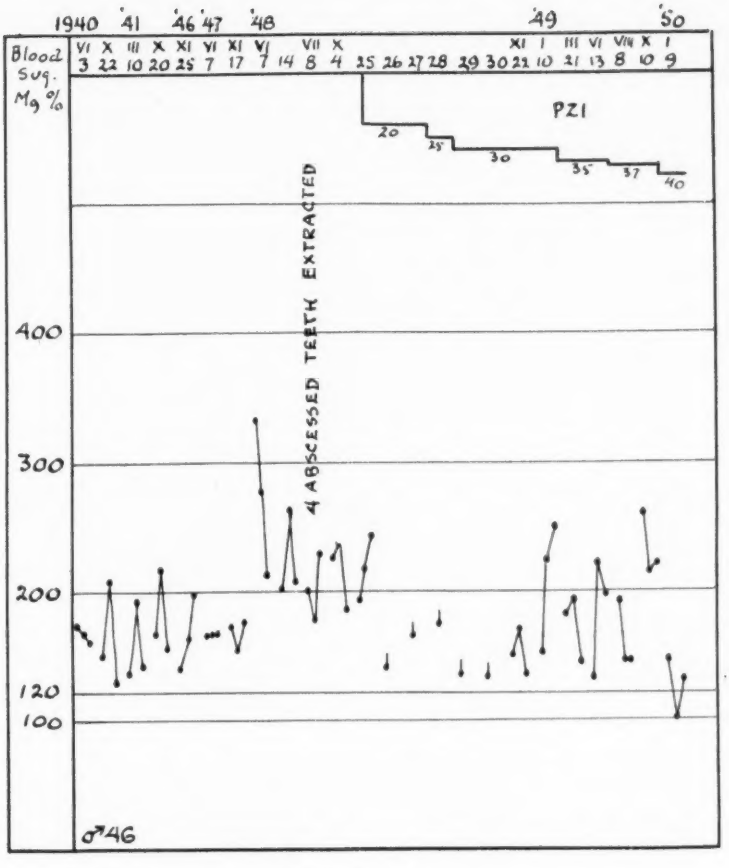

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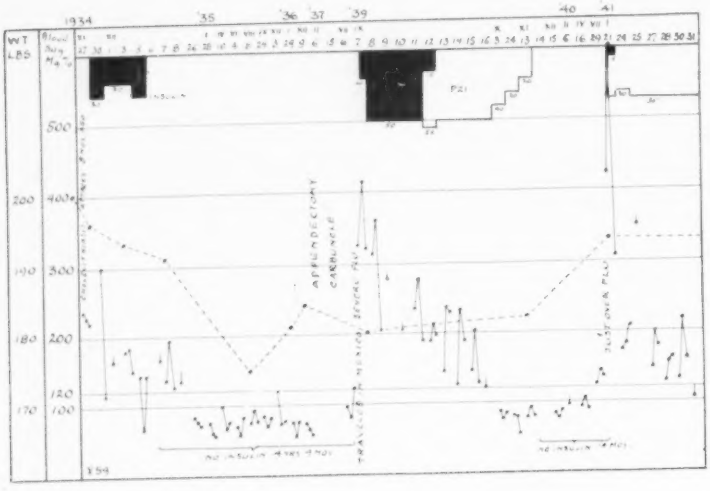


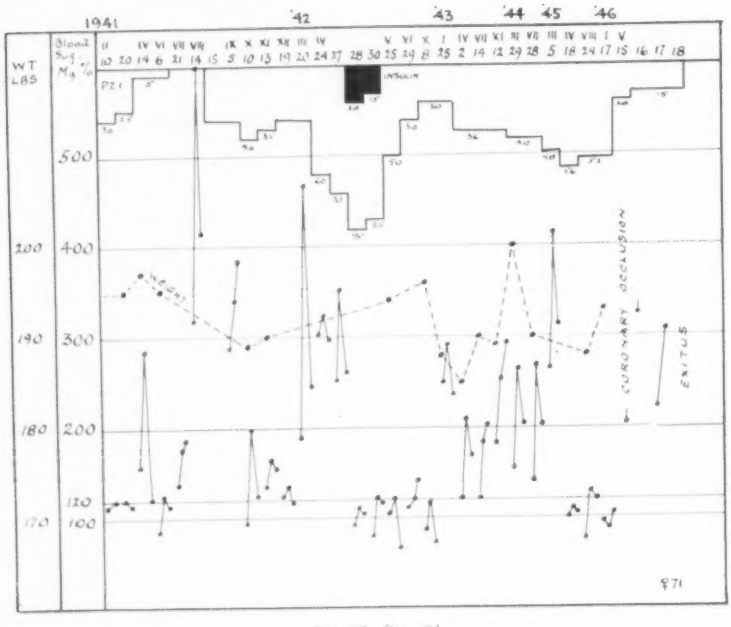


Fig. 31. Case 31.

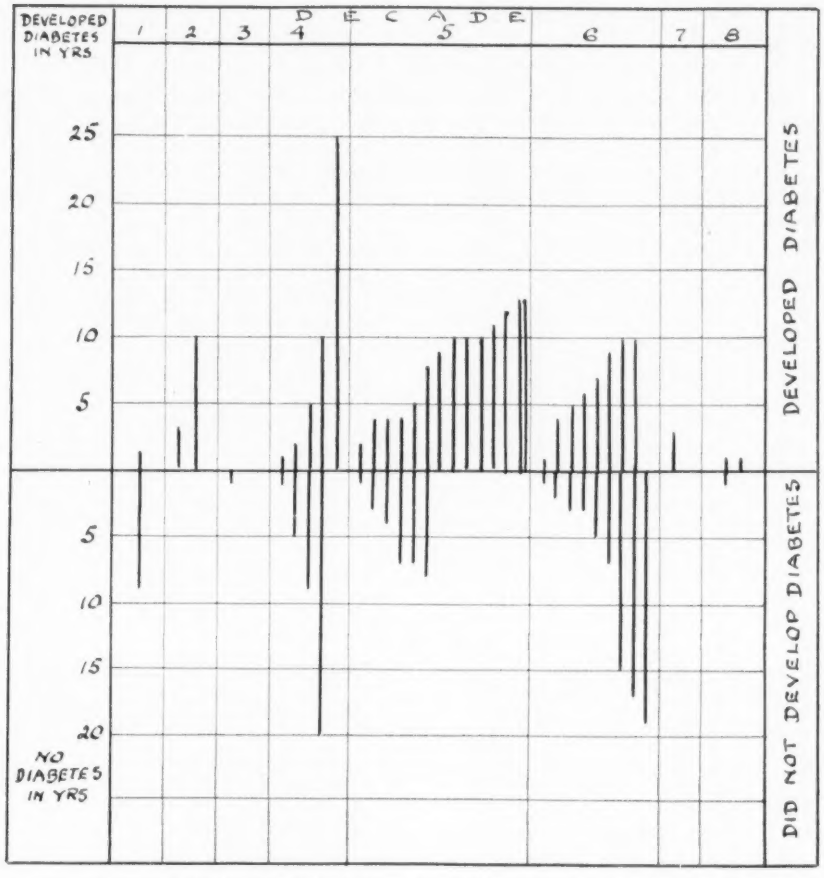


Fig. 32. Ultimate outcome in 55 cases of prediabetic hyperglycemia followed for one to twenty-five years.

need to be re-examined at frequent intervals, if treatment is to be adequate and satisfactory. No recession in diabetes can be accepted as permanent, for as these records and all careful experience demonstrate, recurrence and retrogression are the rule, and not the exception.

The studies here presented also demonstrate quite conclusively that the fasting blood sugar, taken alone, is not a good guide to the actual diabetic status, for it tells only part of the story. Blood sugar determinations made three times a day, before meals, furnish much more information, since they show the time lag in return of the blood sugar to normal, after eating if this is present. Glycosuria may also be actually misleading as to the regulation of the insulin dosage, since it often is not an accurate index of the level of the blood sugar, especially in individuals who have a low renal threshold for sugar.

On the basis of this study of fifty-five cases of mild or prediabetic hyperglycemia, it is possible to formulate a dictum that any deviation from the normal of the blood sugar level must never be disregarded as insignificant. Such a finding requires that the patient be subjected to periodic examinations to determine the glycemic level, continuously, throughout the remainder of his life.

THE VALUE OF LAMINOGRAPHY IN THE DIFFICULT GALLBLADDER PROBLEM

GEORGE LEVENE, M. D. AND CHARLES B. PERKINS, LT. COL., M. C., Boston, Mass.

THE roentgenologic diagnosis of gallbladder disease has attained a high degree of accuracy. This is particularly true in cases with positive findings. However, the same degree of accuracy does not hold in cases found to be "negative" by cholecystography, one of the greatest deficiencies being the inability to detect stones. There are times when precise information about the gallbladder is of vital importance. Such is the case when a decision to operate must be weighed carefully in the balance against signs of heart failure or other severe systemic disease.

Numerous technics have been suggested for the better visualization of gall stones. Films taken in the erect position (1), in right lateral decubitus (2), in inspiration and in expiration (3) and after the administration of prostigmin and other drugs (4, 5, 6) often help to distinguish stones from confusing gas shadows, or to demonstrate stones that cannot be seen on routine cholecystograms. But even these procedures often fail to give sufficient evidence to permit a diagnosis more definite than "suspicious of stones." In such cases we have recently employed laminography with gratifying results. Its application to the solution of some difficult problems is illustrated in the following case reports.

Submitted Sept. 20, 1949.

From the Department of Radiology, Massachusetts Memorial Hospitals, Boston, and Boston University School of Medicine.

Case 1. A woman, 56, years of age, was referred with a chief complaint of pain in the right flank of twenty years' duration, and a substernal burning sensation and vomiting of nine months' duration. On previous hospital entries elsewhere, she had had a Caesarean operation, an appendectomy, suspension of the right renal pelvis to relieve a ureteral kink, and a hysterectomy for uterine fibroids.

Barium studies showed no evidence of disease of the gastrointestinal tract. An electrocardiogram was reported as showing "sino-auricular tachycardia and left ventricular strain." Cholecystograms showed a well filled gallbladder with negative shadows which might be due to stones or overlying gas in the intestines (Fig. 1). Various attempts to identify the negative shadows were not conclusive. Laminograms were made at depths of 4, 5, 6, and 7 cm. from the anterior abdominal wall. The film taken at 5 cm. showed a definite cluster of small stones.

Case 2. A man, 62 years of age, was admitted with a complaint of pain in the region of the xyphoid and umbilicus, radiating to the back, of twenty years' duration. The pain was temporarily relieved by food but soon recurred and was accompanied by nausea. The record of his admission to another hospital nineteen years previously states that his gallbladder was removed at that time. Since then, he has had numerous

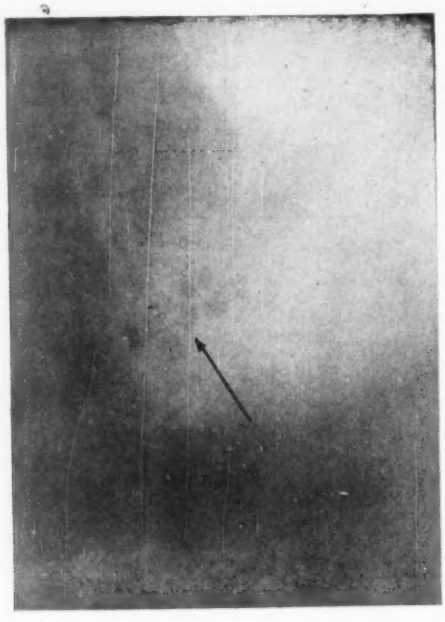


Fig. 1 (Case 1). A. Cholecystogram made 14 hours after the oral administration of dye. It could not be determined from this and other similar films made during the examination whether the negative shadow in the region of the gallbladder was due entirely to gas or stones.

B. Laminogram at a depth of 5 cm. from the anterior abdominal wall shows a cluster of small stones.

Fig. 2 (Case II) A. Plain film of right upper quadrant. No definite shadow of a calculus could be identified. Patient was said to have had a previous cholecystectomy.

B. Laminogram at a depth of 4.5 cm. from the anterior abdominal wall. Two small gall stones are plainly visible.

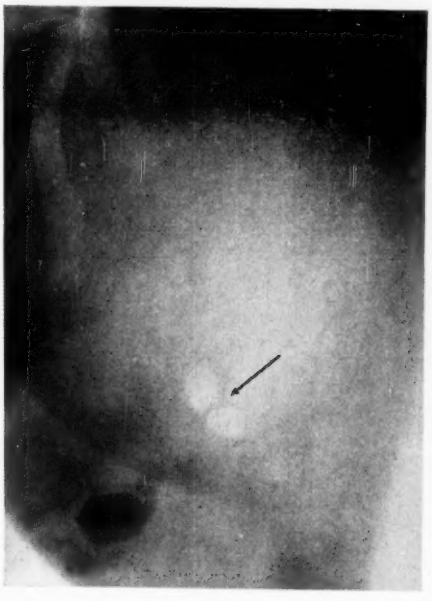
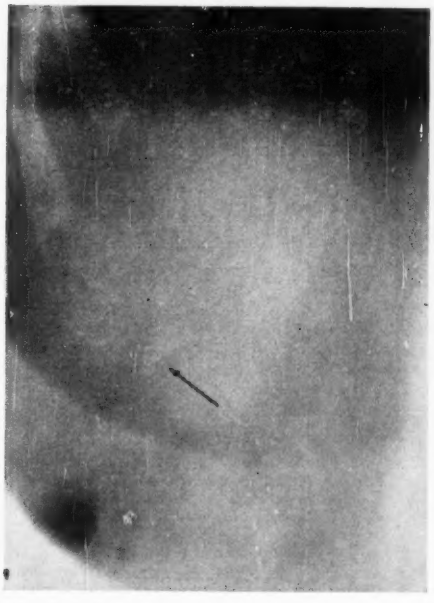


Fig. 3 (Case III) Patient said to have had a cholecystectomy.

A. Laminogram at a depth of 5 cm. from the anterior abdominal wall shows two faceted stones approximately 1 cm. in diameter.



B. Laminogram at a depth of 4 cm. from the anterior abdominal wall shows three additional stones of smaller size.

hospital admissions elsewhere because of the persistence of symptoms. On examination with the barium meal we found an active duodenal ulcer. A plain film of the right upper quadrant showed a faint area of density which might be a calculus. Notwithstanding a history of previous cholecystectomy, laminograms were made at depths of 4, 4½, 5, 5½, and 6 cm. from the anterior abdominal wall. The film at 4½ cm. showed two ring shadows typical of gall stones.

Case 3. A woman, 65 years of age, was admitted with a dull, aching pain and a burning sensation in the right upper quadrant and epigastrium. The discomfort was of sufficient magnitude to interfere with her household duties, for which she was berated by both her husband and her daughter. This contributed toward an emotional conflict in which the patient felt that she was "driven too hard." The patient had had an abdominal operation nineteen years previously at another hospital at which time the gallbladder was said to have been removed. Unfortunately, that hospital record could not be found and the surgeon who had performed the operation had died.

On examination with a Graham test, the gallbladder was not visualized. This failed to answer the question whether the gallbladder was not seen because it was diseased or because it had been removed. A scout film of the right upper quadrant showed no opaque stones. Because of the symptoms, laminograms of the right upper quadrant were made at depths of 3, 4, 5, 6, and 7 cm. from the anterior abdominal wall. The film at 5 cm. showed two faceted stones, almost 1 cm. in size, and the film at 4 cm. showed three smaller stones. At operation, the gallbladder was found to be fibrosed and adherent. It contained five stones.

TECHNIC

The patient lies prone on the table, the left arm by the side, the right hand near the face to assist in suspending respiration by holding the nose when the mouth is shut. The right costovertebral angle is centered to the film. The patient is immobilized with a balloon under a compression band. The most difficult part of the examination is to estimate the depth at which laminograms are to be made. This should be done by the roentgenologist when the patient is in position on the table. It is our practice to first take three films as follows: If the center of interest is estimated to be 6 cm. from the table top, films are made at 4, 6, and 8 cm. These are inspected as soon as they are developed. If, for example, there is a suggestion of stone on the film taken at 4 cm., but not on those taken at 6 and 8 cm., additional films are taken at 3 and 5 cm. For more careful scrutiny of a small area, we not infrequently take films at 0.5 cm. intervals. The average exposure is 100 MA, 65-68 KV, 36 inch distance, 1½ seconds.

CONCLUSIONS

Laminography is a useful adjunct in the roentgenologic study of the difficult gallbladder problem. The examination is, of course, more time consuming than routine roentgenography. On the other hand, if employed early enough in the examination, it may save hours of watchful waiting to see what happens to a suspicious shadow when the gallbladder contracts. Finally, it must be said that if laminography offers a definite diagnosis where other roentgenographic procedures fail, it should be employed more often.

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COMPARISON OF EFFECTIVENESS OF VARIOUS ANTACIDS ON GASTRIC ACIDITY*

S. KRASNOW, M. D., F. STEIGMANN, M. D. AND L. L. HARDT, M. D. Chicago, Ill.

FROM clinical use dating back to antiquity (1), (2) to modern, clinically controlled experiments (3) antacids have been shown to be of value in the medical treatment of peptic ulcer. None, however, have proven completely satisfactory.

In recent years a number of new antacids and combination of antacids have appeared on the pharmaceutical market. The following study is an attempt to evaluate the effectiveness of some of the more recent antacids in neutralizing human acid gastric juice.

*The Hektoen Institute for Medical Research, the Department of Internal Medicine and the Gastro-Intestinal Clinic of Cook County Hospital, the Department of Internal Medicine, University of Illinois, College of Medicine and the Stritch School of Medicine, Loyola University, Chicago, Illinois.

Aided by a grant from the Research Division of the Harrower Laboratories, Inc., Jersey City, New Jersey.

Submitted Oct. 6, 1949.

PROCEDURE

The method of study was based on the technique of Bloomfield and Keefer (4), as modified by Littman and Ivy (5). After a 12 hour fast the patient was intubated with a soft rubber stomach tube and the contents aspirated at 15 minute intervals. Immediately after the fourth sample was withdrawn, the patient was given 0.1 mg. of histamine diphosphate per ten kilograms of body weight, subcutaneously. Aspirations were continued for an additional 90 minutes. The first morning of study the patients were given histamine alone. On the following consecutive mornings a different antacid was given orally at the time of the histamine injections. All antacids were chewed (6). The patients were supplied with expectoration cups and instructed not to swallow saliva. At each 15 minute interval the total gastric content was aspirated, measured

and reinjected into the stomach except for a ten cc. sample used for analysis.

In all cases the free acid and total acid were determined in clinical units using Topfer's reagent and phenolphthalein as indicators and titrating with 0.1 N Sodium hydroxide.

In 18 patients the total output of hydrochloric acid in milligrams, and in three patients the pH were also determined.

The study was conducted on 28 patients. Each was tested on four to six successive mornings. Nineteen of the patients had peptic ulcers (14 duodenal and 5 gastric), proven by x-ray, gastroscopy and/or surgery. Of the remaining nine patients, three had a history suggestive of ulcer, and six patients had unrelated diseases.

The antacids tested, their composition and the number of patients in which each was used is listed in Table I. Although Enterogastrone and Viodenum are not antacids, they were tested for immediate effect on gastric acidity.

TABLE I. NUMBER OF PATIENTS TESTED, ANTACIDS USED AND QUANTITY

Substance Tested	Dose	Composition	No. of Patients Tested
Mucotin (7)*	Tablets II	(aa mucin 0.16 gm. aluminum hydroxide 0.25 gm. Magnesium Trisilicate 0.45 aa 0.5 gm.)	28
Amphojel	Tablets II		24
Okra (8)*	Tablets II	(aa 0.33 gm.)	12
Resinat (9)*	Capsules IV	(aa 0.25 gm.)	10
Resinat plus Mucin	Capsules IV	(aa Resinat 0.25 gm. Mucin 0.16 gm.)	10
Enterogastrone (10)*	Tablets V	(aa 0.5 gm.)	11
Viodenum	Teaspoon II	(aa 2.0 gm.)	10

*References to publications in which these substances were described.

RESULTS

Figure 1 and Table II reveal the reduction in gastric acidity by the various antacids in the histamine stimulated stomach.

As compared to histamine alone, the free acid is reduced for one hour after administration by all antacids. For the four 15 minute intervals after administration no consistent difference in effectiveness between the antacids is readily apparent.

To determine if there were statistical differences in the degree of acid neutralization the results were subjected to statistical evaluation. The "t" values (the probability, P, taken as significant was 0.05 or smaller) were calculated. In Table III the various antacids are compared to Histamine alone. The significant "t" values are recorded as *S* and the insignificant differences are recorded as *NS*. The findings in Table III substantiate the findings in Figure 1 and Table II. At the four 15 minute intervals following administration, all antacids (except Resinat and Mucin at 60 minutes) reduced gastric acidity as compared to Histamine given alone to statistically significant extent. Resinat was also significant at 75 minutes after administration.

A statistical comparison of the above antacids in the same ten patients revealed essentially the same results.

TABLE II. MEAN VALUES OF FREE ACID FOR ANTACIDS AND HISTAMINE IN NUMBER OF PATIENTS GIVEN

Substance	No. of Patients Tested	Time (Minutes) 0 Mean	15 Value	30 of	45* Free	60 Acid	75 in	90 Clinical	105 Units	120	135
Histamine (alone)	28	18	27	24	24	49	63	61	44	38	34
Mucotin	28	20	26	23	21	20	44	51	42	35	31
Amphojel	24	24	25	26	25	28	46	44	35	37	30
Resinat	10	16	21	14	14	23	35	41	32	20	14
Resinat plus Mucin	10	15	13	13	14	21	43	41	39	34	23
Okra	12	19	27	22	19	18	38	47	39	40	37

*Histamine and antacids given

TABLE III. STATISTICAL COMPARISON OF THE EFFECT OF VARIOUS ANTACIDS TO HISTAMINE ALONE (IN CLINICAL UNITS) ON GASTRIC FREE ACID

	Time (Minutes) after Antacid plus Histamine			
Substance	30	45	60	75
Resinat plus Mucin	(S)	(S)	(NS)	(NS)
Resinat	(S)	(S)	(S)	(S)
Okra	(S)	(S)	(S)	(NS)
Amphojel	(S)	(S)	(S)	(NS)
Mucotin	(S)	(S)	(S)	(NS)

(S)—Statistically significant reduction in gastric acidity as compared to histamine.

(NS)—No significant difference.

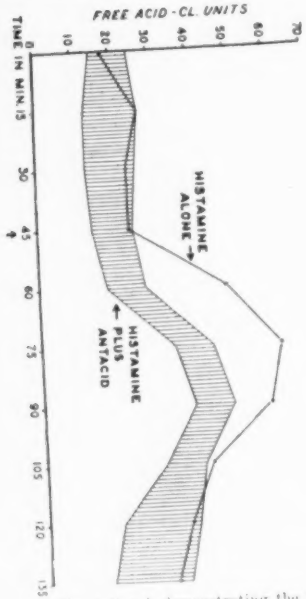

Fig. 1 Graph demonstrating the reduction of Histamine stimulated gastric acidity within a certain range by all antacids.

To compare statistically the effectiveness of the various antacids, they were compared first to Mucotin and then to Amphojel. The results are shown in Table IV. There were no statistically significant differences among the various antacids, except for Okra which is apparently better at 30 minutes after administration.

Enterogastrone and Viodenum in the Histamine stimulated stomach were compared to Histamine given alone in regard to free acid and total volume.

Figure 2 is a composite graph of the mean free acid values in clinical units at 15 minute intervals comparing Histamine, Enterogastrone and Histamine, and Viodenum and Histamine.

Viodenum decreased the free acid at 30 to 60 minutes after administration, whereas Enterogastrone did not alter the free acid.

A comparison of mean total volume at 15 minute intervals is recorded in Figure 3. The total volume of gastric secretion was increased by Viodenum and Enterogastrone in the Histamine stimulated stomach.

DISCUSSION

The comparison of effectiveness of various antacids on human gastric acidity is fraught with difficulties, and the latter place definite limitations on the value of such experiments. Many of the difficulties are inherent in the human subjects being tested, and many are introduced in the procedure used. In the planning and the course of this study many of these variables soon became apparent.

TABLE IV. STATISTICAL SIGNIFICANCE OF LOWERING OF GASTRIC ACIDITY (IN CLINICAL UNITS) AS COMPARED TO (1) MUCOTIN (2) AMPHOJEL

Substances	30	45	60
1. Compared to Mucotin:			
(a) Amphojel	(NS)	(NS)	(NS)
(b) Resinat plus Mucin	(NS)	(NS)	(NS)
(c) Resinat	(NS)	(NS)	(NS)
(d) Okra	(S)	(NS)	(NS)
2. Compared to Amphojel:			
(a) Resinat plus Mucin	(NS)	(NS)	(NS)
(b) Resinat	(NS)	(NS)	(NS)
(c) Okra	(NS)	(NS)	(NS)

(NS)—Not significant

(S)—Significant lowering

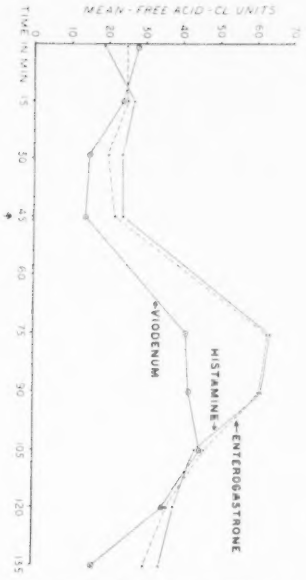

Fig. 2. Graph showing the mean free acid values following Histamine alone, Histamine and Enterogastrone, and Histamine plus Viodenum.

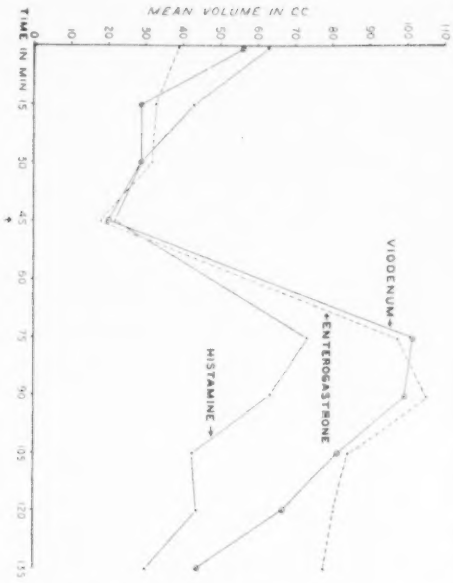

Fig. 3. Graph showing the mean volume in cc following Histamine alone, Histamine and Enterogastrone, and Histamine plus Viodenum.

The fasting free acid in the same patient on successive days varied as much as 72 clinical units. Daily variations in gastric acidity and pepsin have been described by Alvarez (11). Schlesinger et al (12) in a recent study, has also noted daily variations in the gastric acidity of the histamine stimulated stomach.

Although all antacids were chewed, the final particle size, indubitably varies from patient to patient. In the process of withdrawing samples at the 15 minute intervals, the gastric contents were mixed, and thereby dispersed, increasing the effectiveness of the antacids which had a tendency to clump. A ten c.c. sample was retained for analysis at the 15 minute intervals which grossly contained, in spite of mixing, variable quantities of the antacid being tested.

Average clinical therapeutic quantities of antacids were placed in histamine stimulated stomachs, a created condition in which the amount of antacid is small compared to the amount of acid present. As noted by Littman (13), a better comparison may be obtained by using sufficient antacid to neutralize the free acid almost completely.

These factors, therefore, place a limited value on a mixed type of experiment in which purely chemical procedures such as neutralizing acid with base are coupled with biological components.

With due consideration to these variables, this study of effectiveness of various antacids in the Histamine stimulated stomach shows that all of those studied reduce the acidity, and that among them no demonstrable difference is apparent. It is of note that both Enterogastrone and Viodenum increase the total volume of gastric secretion in the Histamine stimulated stomach.

SUMMARY AND CONCLUSIONS

(1) The effectiveness of various antacids in reducing the acidity in 28 human subjects is reported. No demonstrable difference is apparent between the antacids tested.

(2) Differences in clinical results following the therapeutic use of the above antacids may be on the basis of factors other than acid neutralization.

(3) Enterogastrone and Viodenum both increased the total volume of the gastric secretion in the Histamine stimulated stomach.

(4) Several uncontrolled variables and limitations of the method are discussed.

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NUTRITION

VITAMIN E THERAPY IN AMENORRHEA

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THE RECENT medical literature shows an increased number of clinical studies on ovarian dysfunction, especially amenorrhea; and, as might be expected, the purpose of many of these studies was to evaluate the comparative effectiveness of various therapeutic preparations, synthetic and otherwise. It was felt therefore, that perhaps a brief review of two such reports—one for each type of preparation—may prove helpful to those interested. Both reports however, can be best appreciated by a thorough study of the originals.

The first article included in our review is one by Novak (1) in which the author discusses some of the most apparent limitations and risks involved in treating menstrual disturbances with either natural hormone extracts or such synthetic preparations as diethylstilbestrol, particularly the latter. His comments lead to the conclusion that the basic risk in the use of such synthetic preparations lies in the over-stimulation likely to come from either an immediate excessive dosage or from the cumulative effects of a prolonged administration of relatively smaller amounts, and that such over-stimulation, in turn, causes hyperplastic changes in the endometrium and excessive bleeding. The latter, aside from its general physiological aspect, is a disturbing sign in that it may create such a strong suspicion of cancer as to call for a diagnostic curettement; and since such hyperplasia and cancer are frequently found together, it remains a question whether the former is a direct cause of the latter or, more likely, plays a predisposing role. At any rate, the author feels that this hyperplasia-cancer relationship calls for great caution in choosing such forms of therapy in cases of menstrual disturbances.

The second article (2) on which our discussion is based is more inclusive: After mentioning that amenorrhea may result from various causes, including malnutrition, emotional disturbance, neurosis, psychosis, etc., the authors emphasize that their own report is dealing with "amenorrhea as associated with war." The observations were made on the internees at Santo Tomas Internment Camp, in Manila, 1942.

First, however, they submit a brief review of the reports of seven European investigators relative to the high incidence of amenorrhea in central Europe during, and subsequent to, the first world war. By reorganizing their review into the form of a table, we have the following:

AUTHOR	PLACE	YEAR	CAUSES GIVEN
Von Jaworski	Warsaw	1916	Malnutrition and disturbed metabolism.
Dietrich	Gettingen	1917	Malnutrition and hard work; Psychic influence secondary
Bakofen	Berlin	1919	Malnutrition, especially too much ergot-containing grain.
Nilson	Stockholm	1920	Malnutrition, especially a lack of milk, and an imbalance of physiologic salts.
Von Lingen	Lonhgrad	1921	Malnutrition and hard work.
Teebken	Kiel	1928	Malnutrition: low protein and fat.
Graff & Nowak	Vienna	1929	Malnutrition: low protein.

Quite clearly, all seven of these investigators considered the basic cause of amenorrhea to be one of malnutrition—i.e. one of insufficiency or imbalance of essential food factors, with one report giving an excess of ergot as the most probable cause. Such an additional factor as "hard work" would, it seems, merely serve to intensify the malnutrition factor. Only one of these investigators included psychic disturbance as a cause, and then only as a secondary one.

At first glance, these seven conclusions stand in

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direct contrast to those formed by Whitacre and Barrera concerning their causes in the Manila Internment Camp. In the latter instance, the authors state that, in many of their patients, the disturbance (amenorrhea) came on too abruptly and too soon after internment to be attributed to food deficiency; and that one must therefore look for other causes. The most plausible of these were worry, fear and emotional shock due to the intense air raids and bombings.

Assuming these causes to be the correct ones, the authors felt "it desirable to study the effect of such shock on the ovarian and anterior pituitary-like gonadotropic excretions in the urine." Albino rats of the Wistar strain were used in the tests. Even though the tests, due to a shortage of animals, were fewer than desirable, the authors nevertheless felt satisfied that they proved the *presence* of the anterior pituitary-like substance (gonadotropin), and the *absence* of estrogen, which would indicate that the amenorrhea did not result from an inhibition of the pituitary function, but from a direct suppression of the ovarian functions.

To substantiate their deduction that this dysfunction was induced through nerve channels, emotional shock etc., the authors emphasize that ovarian function is under the influence, not only of the endocrine glands, but also of the autonomic nervous system. This latter fact, especially when viewed in relation to the nerve-wrecking effects of the previous air raids, seems to form a strong link in the authors' conclusion that, in the cases reported by them, the amenorrhea resulted from an ovarian dysfunction (metabolic disturbance) induced by emotional shock, and not by malnutrition. This apparently well-substantiated deduction does not, of course, preclude the probability that amenorrhea may also result from other causes, especially so in view of the mentioned European reports which appear equally conclusive in regard to malnutrition as the cause. On one point, however, the Manila report is more specific; it eliminates pituitary dysfunction as a preliminary phase in the chain of events leading up to the amenorrhea. It would be of interest to know whether or not that also holds true in cases in which malnutrition is considered the basic cause.

Reflecting for a moment on the two mentioned causes of amenorrhea, namely malnutrition and emotional shock, the following comments may be in order: All body functions depend on a continuous supply of all essential food factors, and when this supply fails, in part or in whole, a proportionate functional disturbance is inevitable. That is, barring infections, etc., and with other things equal, the severity of such functional disturbance, tends to be proportionate, say, to the extent and duration of the food deficiency. However, "other things" are seldom, if ever, equal, and consequently the functional disturbances, both in kind and severity, vary according to such factors as age, sex, occupation, and the *prevailing physical environment*. This last factor—the prevailing physical environment—was apparently the inciting agent in the Manila cases; while, as already mentioned, malnutrition was considered the chief cause in the European report. It might be emphasized, however, that while the conditions in Europe during, and subsequent to, the First World War did not include the most extreme of the nerve-shattering features of Manila, this does not imply that the less severe ones were also absent, and that these lesser ones did not play a part in the onset of the widespread incidence of amenorrhea. Indeed, it would be difficult to believe that any individual, especially a woman, could pass through such an ordeal as World War I and its aftermath, without experiencing a rather continuous feeling of worry, fear, and emotional upset.

As far as the two reports on amenorrhea are concerned, the chief differences between the prevailing physical environments in Europe (World War I) and in Manila (World War II) may be summarized as follows: In Manila, the patients experienced little, if any, food deficiency, but were subjected to a brief and very intense sensation of worry, fear, and emotional shock; while in the European area they experienced a prolonged food deficiency and perhaps an even more prolonged period of worry, fear, and intermittent emotional shocks. The psychic disturbance, then, was definitely present in both Europe and Manila (comparatively mild but prolonged in the former, intense but brief in the latter), while malnutrition is assumed to have been present in Europe, but not in Manila.

The implications of these assumptions call for further comments. But first one more difference should be noted, namely that the duration of the subclinical period, prior to the onset of the amenorrhea, varied inversely as the intensity of the psychic disturbance and/or emotional shock; that is, the stronger the shock, the shorter the preclinical period. In Europe, the emotional shock was *comparatively* mild, and the preclinical period long; in Manila, the reverse was true. The Manila report however, does not permit any deductions regarding a similar relationship between *malnutrition* and the duration of the preclinical period because, according to the authors, food deficiency was not an inciting agent in the cases reported by them.

However, on the basis of our deductions a few paragraphs back, to the effect that the *severity* of a functional disturbance induced by malnutrition is proportionate to the food deficiency, it seems also safe to deduce that the subclinical period, prior to the onset of such a functional disturbance, varies inversely as the food deficiency; that is, the greater the food deficiency, the shorter the subclinical period. In fact, both of these deductions concerning the interrelationship between malnutrition and/or emotional shock and the subclinical period appear well-nigh axiomatic. Who, for example, would refute that the greater the food deficiency, the sooner the onset of the resulting functional disturbance? In the case of emotional shock however, the picture is less clear to most people, and it seems appropriate therefore to take this means to clarify the issue by emphasizing the supporting evidence presented in the Manila report.

No matter how axiomatic the above deductions may appear, they are nevertheless subject to certain modifications: It is evident to even the most embryonic investigator that in considering the relationship between, say, malnutrition and the preclinical period, no definite (quantitative) evaluation is possible unless any other similarly-acting factor (in this case emotional shock) is held constant or entirely eliminated: The closest approach to this desired condition was evidently in Manila where, according to the authors, the problem of malnutrition was not sufficient to be

included in their calculations. If this be correct, the reported results indicate that an emotional shock, if sufficiently intense, may in itself be enough to, not only precipitate an attack of amenorrhea, but does so within a much shorter period than that required to produce similar results by means of a food deficiency, partial or total.

The European situation however, was not so clear-cut. There the cause was two-fold: An emotional upset (worry, fear, etc.), and malnutrition. The latter, to be sure, was the cause selected by the investigators, but as we have shown above, the psychic factor cannot logically be left out. With two factors thus present, it may be conceived that neither factor was by itself great enough to induce such a functional disturbance as amenorrhea, but that the prolonged and combined effects of both factors could ultimately add up to the potency required to produce such a disturbance.

At first glance, both of these factors appear quite independent as to cause. But this holds true only in part, for worry, fear and emotional shock may definitely interfere with nutrition—not through the external food supply perhaps, but through an inhibitory influence on the digestive process; and reversely, hunger and starvation (economic insecurity) can hardly be eliminated from conditions tending to cause worry and fear. Under *modern* warfare however, as so well illustrated by the Manila report, hunger is not so likely to be the *major* cause of worry, fear and emotional shock as was the case in former wars. One may assume however, that regardless of their source, the conditions giving rise to malnutrition and emotional upsets are not constant in force, but fluctuant; with the result that their *combined* effect (potency) is likewise a fluctuating quantity. The latter, in turn, would then exert its influence in a similar wave-like fashion, and the total potency, at any given time, would be equal to the sum of the then co-existing amplitudes of the two factors.

If these "waves" then, happen to superimpose, or synchronize, crest to crest, the required height (potency) could be achieved in a comparatively short (subclinical) period; while if they synchronize "crest to trough," the required height would not be attained for a much longer time, thus giving rise to a correspondingly prolonged subclinical period. In fact, with proper synchronizing, both factors could be active in the subclinical zone for a considerable period without overcoming the existing resistance to precipitate a clear-cut attack of amenorrhea.

It is well to remember however, that the mentioned resistance is not a constant for the following reasons: Since food deficiency is one of the factors at work, it seems evident that as the subclinical action continues, malnutrition increases and the individual's resistance decreases, until sooner or later the resistance-threshold is lowered to a point where fluctuating nervous impulses resulting from psychic disturbances, "jump the gap" inciting actions derogatory to the existing normal physiological functions. In the cases discussed, this derogatory action is an inhibitory effect on the production of estrogen, resulting in amenorrhea. The situation so far described, may be pictured in brief as follows:

1. Under normal conditions, the production of estrogen is dependent on several factors, such as: a sufficient food supply, the sympathetic nervous system, endocrine secretion, etc. For the present however, only the two first-named are being considered.

2. The transformation of appropriate food material into estrogen is a cellular function which, like other cellular functions, is initiated and controlled, directly or indirectly, by nervous impulses. Any distortion of these impulses, beyond the normal threshold range, either in frequency or potential, may be expected to produce a corresponding disturbance in the estrogen production, even though all essential food material is present. The Manila cases would seem to fall in this category. Conversely, a similar disruption of estrogen production is equally certain if, with the nervous control intact, the essential food material is withheld. Obviously, estrogen, like all other material things, comes under the law of conservation of energy and matter: that is, it can be produced only from other matter; not from nothing. If that "other matter," in this case proper food, is not present, the inevitable result is: no estrogen!

3. The condition most commonly encountered however, is no doubt that of a *partial* disruption of both the nervous control and the food supply. If the disruption is moderate in both cases, the resulting condition may continue unnoticed (subclinical) for a long time; but the food deficiency will ultimately reduce the individual's resistance to a point where the distorted nervous impulses will "jump the gap," causing a clear-cut abnormal function. Many, if not most, of the reported European cases no doubt fall in this category, as do probably also most of our peace-time cases of ovarian hypofunction.

The latter deduction seems justified on the following bases: 1—the numerous authoritative reports, by both private and govegrnmental investigators, on the widespread occurrence of nutritional deficiency (See Bulletin No. 109 of the National Research Council, 1943, National Academy of Sciences, Washington, D. C.); and 2—the generally accepted view that present social conditions are becoming more and more conducive to worry, fear, and emotional upsets. Quite spontaneously, this raises the question: What's the remedy? Common sense, rare though it be, directs that as long as a dysfunction has not progressed beyond the point of spontaneous reversability, upon the removal of the cause, then the most sensible procedure is to eliminate the cause or causes. As previously indicated, in amenorrhea we may assume two causes. On the basis of their mode of action, these may be viewed as direct and indirect. By *direct* action, the physical environment produces a state of worry, fear, and emotional upset; while certain essential food factors, *due to their absence*, are the *indirect* cause of a lowered resistance.

The remedy then, is also two-fold: 1—removing the aggravating phases of the physical environment; 2—supplying the missing food factors. The ideal procedure would naturally be to eliminate both causes; but in case of a choice, the selection, as far as possible, should fall on No. 2—that is, to supply the missing food factors, because an individual can better adjust himself to an altered physical environment than he can to a deficiency of essential foods. The food is *essential*; the previous physical environment may, or may not, be.

Sufficient food, then, is the primary requisite, though

it is well to remember that the mere consumption of food does not necessarily remedy or prevent malnutrition. The food must be digested, absorbed, transported to the cells and there "ignited." But even that is not all; it must, first of all, contain *all* the elements essential for the structural and functional completeness of the individual; and secondly, these elements must come in combinations assimilable by the individual. For example, if the food contains all the essential parts except iodine, thyroid deficiency would inevitably follow. Similarly, other food elements, or special combinations thereof, serve as "specifics" for other body functions, both local and general. Some of the vitamins, for example, are now considered as such "specifics," and the verification of several more such relationships is no doubt in the offing.

In fact, in view of various reports including the one from Manila by Whitacre and Barrera, one feels justified in asking whether such relationship has not been proven in the case of vitamin E and the ovarian production of estrogen. Indeed, the report from Manila states that such small amounts as 20 drops of Wheat Germ Oil per mouth, three times per day, for ten days, restored the menses in eight patients in a group of ten, and one of the remaining two "experienced severe lower abdominal cramps, but no bleeding." This left only one of the ten unaffected. Estrogen was proven absent in two patients selected for such tests just prior to the feeding of the Wheat Germ Oil; and it was proven present subsequent to the treatment.

It should be recalled here however, that the authors themselves conclude that the favorable results obtained, probably came through psychic rather than physiological channels. To us, such an interpretation appears quite untenable, but no one, we are sure, can or will dispute the authors' right to draw their own conclusions, regardless of how much these may differ from those formulated by others from the same data. In view of the information available on other vitamins, each of which acts through physiological, or biochemical, channels, one finds it difficult to assume a different, (psychic), channel for vitamin E. It seems more logical to conclude that, just as iodine for example is an essential food for the function of the thyroid, so vitamin E is essential for the ovarian function; both functions of course, being physiological, not psychic, in nature, though it is obvious that such functions may be *modified* through "psychic" channels. However, any such division of thought as to the probable channels of vitamin E activity is less significant than is the fact that the desired results were actually obtained. After all, it is results that count, especially in therapeutics.

The authors state that "good health, both physical and mental," is a prerequisite for normal ovarian function. In this we fully concur, and would add that the same prerequisite also holds for other organic functions. We believe too, that the authors in turn will concur with us to the effect that, just as there can be no *all-round* good health during a *general* deficiency of essential foods, just so there can be no normal function of a *special* organ, ovarian or otherwise, during a deficiency of *its* essential food. If the latter deduction conforms to good reasoning, as we believe it does, it indicates that, next to an organic structural perfection, food sufficiency in all its essential parts, is a basic prerequisite for the normal function of each and every organ, the sum total of which means good health. It might be added, of course, that "an organic structural perfection" is originally dependent on a food sufficiency.

If in connection with the above, one recalls the environmental influences, then the average non-complicated case of amenorrhea may be viewed as resulting from a battle between the onrushing distorted nervous impulses and the co-existing ovarian (biochemical) resistance, the latter having lost the battle. If one assumes this resistance to be normal, then the logical therapeutic approach would be to rectify the incoming nervous impulses. The applicability of this procedure however, may frequently prove limited since it depends on a prior modification of the physical environment, which in itself is a difficult assignment.

On the other hand, if the ovarian (biochemical) resistance is not up to par, then the logical therapeutic approach would be to re-establish the same by supplying the missing food factor(s) which, in this case appears to be vitamin E. If both the nervous impulses and the resistance are distorted, it logically follows that both be treated as conditions demand and permit.

It is well to remember however, that prevention is better than cure, and that in the case before us, a rational and effective preventive would consist of a wholesome diet, supplemented if necessary, with vitamin E. Regardless of whether such a supplement is administered as a corrective or preventive measure, it may always raise the question of possible over-consumption. There is, of course, no denying that overeating is one of man's weaknesses and that various ills do arise therefrom; but in many cases such effects appear to come chiefly from the consumption of unbalanced foods; that is, from foods deficient in one or more essential factor. In case of well-balanced foods, the margin of safety is normally quite large, and ill effects from over-consumption are no doubt much more remote than usually claimed, and this margin of safety should hold true, even more so, in the consumption of food-factors already deficient, as vitamin E appears to be in such ovarian dysfunctions as amenorrhea.

Then, too, as far as an excessive accumulation of vitamin E is concerned, it is apparently prevented by some special physiological function as indicated in a report by Wechsler (3) et al. They state that the highest vitamin E level is around 2.0-2.5 mg. per 100 cc of blood serum, and that this "cannot be surpassed even by the administration of liberal amounts." They also submit the interesting fact that it was by oral administration that the vitamin E serum level was brought to its peak; patients receiving intramuscular administration only, experienced a drop in the blood tocopherol. All in all, the reviewed data would tend to render support to the procedure followed by Whitacre and Barrera in Manila, namely—oral administration, in amounts indicated, which in their cases were taken to be 20 drops of Wheat Germ Oil, three times per day, for ten days.

At this point it seems appropriate to give support to the foregoing by adding a part of the closing paragraph of the chapter on "The Reproductive Organs" in the epoch-making book "Studies in Deficiency Disease" by Sir Robert McCarrison, M.D. Page 143:

"These observations are of significance in gynaecological practice. Disturbance of ovarian function requires consideration from several points of view: (1) From that of nutrition in general; (2) From that of the vitamin-content of the food in particular; and (3) From that of functional derangement of other endocrine organs consequent on food deficiencies. The application in practice of the information recorded in this chapter should yield valuable results."

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ABSTRACTS ON NUTRITION

MATTMAN, P. E.: *Gout, a common disease.* (Alex. Blain Hosp. Bull., 1949, 8, 4, 136-140).

The thesis of the author is that gout is not an uncommon disease in Michigan, in support of which he describes 10 cases seen recently in one year, representing nearly 5 percent of all patients having joint disorders. The diagnosis rested partly on clinical manifestations but was clinched by finding elevated values for uric acid in the blood. The first joints involved almost invariably were the metatarso-phalangeal. As a rule prompt response was obtained by treatment involving rest, forced fluids, low purine diet, salicylates and colchicine gr. 1/120 every hour until the attack subsided or diarrhea occurred. Repeated courses of colchicine were employed every 24-48 hours when required. Among all affections of joints, gout yields most readily to the intelligent therapeutic efforts of the physician.

CRAMPTON, C. W.: *Nutrition, geriatrics and the physician.* (Nutrition Rev., 7, 10, 289-290).

A man at 60 may be "young" or "old" depending on his past diet, powers of digestion, absorption, etc., and the commonest deficiencies are calcium, iron, proteins, B complex and A. Nutrition surveys are inaccurate but should be made on individuals. The author seems to regard constipation as serious. He also relies on the urinary excretion of methylene blue as a rough test of renal function. In geriatries, the importance of good food and nutrition requires emphasis.

SEAL, S. C. AND BANERJEA, R. K.: *Incidence of gastro-intestinal disorders in relation to the drinking water sources in a rural area in Bengal.* (J. Indian Med. Assoc., 18, 9, 319-326).

Briefly, bacillary dysentery is the chief cause of digestive infections in the Singur area, but the authors could not determine that the ordinary sources of water supply were responsible, and feel that the infection is usually obtained in other ways.

SHORVON, H. T. AND RICHARDSON, J. S.: *Sudden obesity and psychological trauma.* Brit. Med. J. Oct. 29, 1949, 951-956.

The authors have 12 cases, of which 3 are described, in all of whom rather sudden weight increases occurred following psychological trauma. While one usually thinks of worry and emotional concern as more likely to induce weight loss, the authors show that, in some individuals, actual obesity may result. It is felt that the obesity is largely due to water retention and the authors introduce an interesting idea, viz., that strong emotion, by acting upon the hypothalamic nuclei, may release from the pituitary its anti-diuretic substance. At all events, suitable psychological treatment in these cases gave remarkably good results in getting rid of both the distressing emotions and the extra poundage, even without the use of diets or dextro-amphetamine. The form of treatment used was a combination of psychotherapy with abreaction under ether. (Abreaction is the mental reliving of a former actual experience, and serves as a catharsis.)

ROSEN, H. AND LADZ, T.: *Emotional factors in the precipitation of recurrent diabetic acidosis.* Psychosomatic Med. 1949, XI, 4, 210-215.

A careful study of 12 diabetic individuals who were noteworthy for the frequency of their lapses into acidosis, revealed the interesting point that hospitalization frequently was sought as a refuge and an escape. In order to gain admission, insulin and diet were often purposely omitted and even self-infection was practised. Some of the patients, rebelling against "authority", were actually seeking to end their own lives by such means. By cutting down on authoritativeness and expressing confidence in the patient to follow instructions, the authors hope that improvement may result in these cases.

BEST, C. H., HARTROFT, W. S., LUCAS, C. C. AND RIDOUT, J. H.: *Liver damage produced by feeding alcohol or sugar and its prevention by choline.* Brit. Med. J. Nov. 5, 1949, 1001-1006.

Using an adequate basic diet in white rats, it was found that supplementation by 15 per cent alcohol in place of drinking water, or by isocaloric amounts of sugar solution, resulted in fatty changes or fibrosis of the liver. The hepatic changes were thought to be due to an imbalance between caloric intake (increased by either alcohol or sugar) and the supply of vitamins. The high caloric intake apparently induced a specific deficiency when the basic diet was marginal with respect to any one vitamin. Alcohol or sugar in excess supplants choline-containing foods. It was found possible to protect the liver from damage by giving adequate amounts of choline or its precursor, methionine (free or in casein). Thus excess caloric intake may induce a specific choline deficiency. It is not known whether these facts are applicable to man or not.

DECKER, J. W.: *Micro-determination of blood iodine.* Harper Hosp. Bull. 1949, 7, 6, 321-322.

Using a modification of Salter's original micro-method for blood protein-bound iodine, the normal range of blood iodine was found to be limited from 2 micrograms per cent to 4 micrograms per cent. Hypothyroids showed values from 2 micrograms per cent down to zero. Hyperthyroids gave values from 4 micrograms up, with a mean average of 6 micrograms per cent. Such tests, combined with BMR's and other tests increase the accuracy of the diagnosis.

BARGEN, J. ARNOLD: *A method of improving function of the bowel: the use of methylcellulose.* Gastroent. 1949, 13, 4, 275-279.

The author gives somewhat unstinted praise to methylcellulose and reports finding that tablets of this substance dissolved in luke warm water and administered by the mouth constitute a rather remarkable aid in inveterate constipation and also bring comfort and relief in spastic states of the colon, whether associated with diarrhea or constipation. The remedy also is valuable in regional ileitis and in cases where stomas have been made. However in advanced ulcerative colitis, no similar benefits were noted. Once bowel function has been restored, the dosage may be reduced. After the solution or suspension of methylcellulose enters the tract, no bulk forms until the material has reached the lower ileum where it undergoes concentration by the absorption of water from it.

DODD, K. AND RAPOPORT, S.: *Hypocalcemia in the neonatal period.* (Am. J. Dis. Child., 78, 4, 537-569).

Thirty-three instances of hypocalcemia of the new-born were encountered in the Children's Hospital of Cincinnati from 1937 to 1947. In a recent study of the relationship of calcium level to clinical symptoms, 21 infants with signs suggesting tetany were observed. Vomiting, convulsions, edema, cyanosis and hemorrhage were the severest symptoms, and in those infants with tetany-like symptoms, the blood calcium varied between 6 and 9 mgm. per 100 cc. The phosphorus was above 8 mgm. in one-third of the children. Hypocalcemic tetany in the newborn may be serious and administration of calcium is urgent.

CADE, J. F. J.: *Lithium salts in the treatment of psychotic excitement.* (Med. J. Australia, 36, II, 10, 349-352).

Rather remarkable and dramatic improvement was ob-

tained in a number of cases of chronic and acute mania through the administration of lithium salts. Many cases which had been manic for years were controlled in a matter of weeks and enabled to leave the institution and return to work. All this leads to the speculation as to whether lithium, a trace element, could, through a lack of its ions, actually cause mania. It may be an essential trace element. The author feels that the proper use of lithium in restless, mental defectives would be as effective as leucotomy and preferable. (Caution: one ought not to use lithium salts in these cases without consulting the original article for dosage, for, if given in excess, the drug may prove fatal).

BEELER, J. W., TILLISCH, J. H. AND POPP, W. C.: *A new drug in the treatment of radiation sickness.* (Proc. Staff Meet. Mayo Clin., 24, 19, 447-483).

A preliminary study on the treatment of radiation sickness in a series of 82 patients using a new drug, dramamine, showed a significantly higher percentage relief of symptoms than a control series of 23 cases. It is felt that this inexpensive drug can safely be used both as a therapeutic and prophylactic agent in radiation sickness. A combination of dramamine and pyridoxine in the more severe cases gives the therapist an additional agent of great value.

KARN, H.: *The use of streptomycin in the treatment of progressive post-operative gangrene of the abdominal wall.* (New Zealand Med. J., 48, 266, 380-384).

The rapid response to streptomycin in 24 to 48 hours with marked clinical improvement after the exhibition of all other antibiotic drugs had failed, is described in 3 cases of progressive post-operative gangrene of the abdominal wall. Theoretically the disease is caused by the symbiosis of two bacteria, a staphylococcus aureus and a micro-aerophilic anerobic streptococcus. Presumably streptomycin kills one of them and appears to inactivate the combination in 24 to 48 hours. No reports of such rapid response to therapy have previously been recorded.

RAO, B.: *Peritonitis following non-penetrating trauma.* (J. Indian Med. Assoc., 18, 8, 281-282).

A man of 40, struck a blow on the abdomen, died 59 hours later of peritonitis due to *B. Coli*. Obviously he suffered a perforation of the pelvic colon, but like so many of these cases, he did not report for treatment until nearly 24 hours after the injury, and so operation was delayed. The medico-legal aspects of these and similar cases are interesting, because it is necessary to decide if the inflicted blow was a sole or partial cause of death. (The tendency in America would be to consider the assault as part of the cause of death, for it is well known that even a minor blow to the abdominal wall may produce perforation of the gut. The judgment would depend somewhat on the circumstances attending the assault).

EDITORIAL

FOOD, POPULATION AND WORLD POLITICS

Bertrand Russell's paper, "Can a Scientific Society be Stable?", read before the Royal Society of Medicine, and published as the leading article in the December 10, 1949 issue of the British Medical Journal, is cast in his usual lucid prose, and contains interesting conclusions drawn from his study of the effects of science upon the stability of human society. Its chief intent, however, easily boils down to his single statement,—

"I think it is the duty of all who are capable of facing facts to realize, and to proclaim, that opposition to the spread of birth control, if successful, must inflict upon mankind the most appalling depth of misery and degradation, and that within another fifty years or so."

No one will deny that there are already too many people in the world in proportion to the available food supplies, but not everyone will agree that Bertrand Russell,—or anyone else,—has the solution of this grave difficulty. It is possible that emergency solutions of parts of the problem are all that may be expected. The distinguished mathematician, philosopher and exponent of logical analysis, for whom most readers have the highest respect and a warm regard, feels that a world society under the multiplex influences of science, as ours is, cannot be stable unless there exists a world government to enforce the rationing of food to the nations. Such a government "should deal out the world's food to the various nations in proportion to their population at the time of the establishment of the authority. If any nation subsequently increased its population it should not on that account receive any more food. The motive for not increasing population would therefore be very compelling."

Russell's plan is really a controlled world society on the most ambitious scale imaginable. We grant that birth control education exerts an appreciable influence on population increase, but in addressing ourselves to the point at issue, without reference to the wide spread prejudice against birth control or to the moral issue involved, we feel that Russell's plan contains basic weaknesses and insuperable difficulties. Provided that such a global scheme could be accomplished at all, it would immediately result in a universal black market in foods, and such unlawful procurement would be completely condoned through sympathy with the hungry and dislike of the unpopular regulations.

Reliance on birth control education, buttressed by food penalties for excessive procreation, represents an impossible type of procedure. Wherever penalties are provided there must be a law against the commission of the act invoking the penalties. The hypothetical world government would be at once forced to pass such a law making it an offense for any family to have more than a certain number of children, and penalizing *that particular family* by the withholding of food from them. Obviously no national, state or provincial government would be able to enforce such a penalty.

Owing to the very slow results of birth control education, the global authority, in order to consolidate its urgent aims, would almost at once find it necessary to resort to measures other than education, or else abandon its efforts. Russell avoids mention of this contingency, although it logically follows from the establishment of a world authority bent on reducing the human population. The simplest and cheapest effective procedure would be the ligation of the *vasa deferentia* in selected categories of males, since Russell is opposed to infanticide and starvation on grounds of human sympathy. This surgical procedure might be tolerated among institutionalized psychotics and feebleminded citizens, but once a criterion for a broader selection of subjects were adopted, whether on an economic, a psychological or a physical basis, human liberty would be considered seriously infringed upon, and no democratic government would have the temerity to accept it. Thus the hypothetical world government would at once, and of necessity, become despotic in the exercise of its powers over the individual. Surely, if starvation itself had not produced a war of conquest, such laws would provide ample inspiration for wars of liberation.

We submit that the most effective weapon against over-population is that process which we call,—civilization. Whatever civilization means, it at least means fewer children. At present the western nations are not contributing much to the daily increase of 80,000 in the world's population. Economic restraints and cultural influences in an advanced society greatly depress the birth rates. Civilized man, even in a scientific age, succumbs unconsciously to the conquering drive of abstract ideas, which noticeably divert his attention from the exercise of the procreative faculty. If we could civilize the entire world we would at once accomplish our purpose, but unfortunately, civilizing is much too slow a process to meet the deadline to which Russell refers.

On the national level, planned societies are not turning out too well these days, so that we could not expect much from the global control of a biological function of man. The logical and mandatory philosophy of the hour is regional self-preservation. Specifically, the Western nations must find a way of preventing the inroads of food-hungry and power-hungry hoards upon our territories. This military duty may remain urgent for half a century or more. To resist these millions bent on pure plunder the West needs,—not birth control, but its opposite. We need more children, not fewer, if we value liberty and the treasures of civilization. All natural laws justify us in protecting ourselves from the instability, which, as Russell shows, arises from the population crisis of the world. It is not necessarily true that the sympathetic distribution of our food and wealth to starving areas will eventually protect us from the military encroachment of vital populations upon us. Birth control dictated by a global government is, in the light of our current social conciousness, bizarre and unacceptable. The breeding of children is natural, and so also is self-preservation.

BOOK REVIEWS

CLINICAL NUTRITION. Norman Jolliffe, M. D., F. F. Tisdall, M. D. and Paul R. Cannon, M. D., 925 pages, Paul B. Hoeber, Inc., New York, 1950, $12.00.

This volume, which could not have been published at its sale price except for assistance from the Food and Nutrition Board of the National Research Council, probably exceeds in scope and usefulness any single work ever published on the subject of clinical nutrition. All profits from its sale will be returned to the Board to support its research projects. First, the pathogenesis of deficiency disease and methods of diagnosis (clinical, laboratory and x-ray) are presented in sufficient detail. Second, the various nutrient elements are dealt with somewhat individually, each by an authority who has spent most of his life-time upon pertinent investigations. Finally treatment and prevention, dietotherapy and food tables, weight tables and "dietary patterns" complete the work. The book is profusely illustrated with a great many beautiful color plates of lesions.

Apart from its value as a practical text, some of the chapters, particularly those by Jolliffe, serve to give the subject of nutrition a very broad orientation. The following quotation indicates how easily and naturally food becomes or may become a weapon for political or warlike purposes: "The pressure of peoples to obtain and insure dietary adequacy has been a frequent cause of mass migrations and of war." It is Jolliffe's conclusion that even in America, where food conditions are much better than elsewhere, unsatisfactory diets are widespread throughout the nation. Our national intake of thiamine, riboflavine and niacin are particularly below optimum by any acceptable standard. The excessive consumption of highly refined foods has contributed to the poor nutritional status of our country, although this has been in part remedied by the enrichment of bread and flour.

Not only is Clinical Nutrition an invaluable addition to the study-shelf of any physician from the purely technical aspect, but it is also a monumental contribution to the entire conception of human nutrition and its bearing on health, disease and world politics. It is a most worthwhile investment at $12.00.

WATER AND SALT DEPLETION. H. L. Marriott, M. D., 80 pages, Chas. C. Thomas, Springfield, Ill., 1950, $2.00.

Perhaps this little volume presents in a concise form all that is necessary for the clinician to know about the diagnosis and treatment of water and salt depletion. In cases where the patient has failed, for any reason, to imbibe sufficient water, we are dealing purely with a water deficit. In cases in which there has been excessive loss of secretions, such as vomiting especially, we are dealing with salt depletion as well. This is an over-simplified epitome of the treatise. The book is valuable particularly since it helps the physician to know when to give water, isotonic saline or hypotonic saline.

FAMILY FARE: FOOD MANAGEMENT AND RECIPES. U. S. Dept. of Agriculture. (For sale by the Superintendent of Documents, U. S. Gov't. Printing Office, Washington 25, D. C., 25 cents).

This 96 page book, prepared by the Bureau of Human Nutrition and Home Economics, is intended to acquaint the lay person with the fundamental nature of foods, particularly the nutritional aspects of diet, and also offers advice with respect to "smart buying" of commodities. The bulk of the book contains recipes and cooking instructions. The physician might suggest this book to the normal housewife who desires to delve into the problem of nutrition from a practical standpoint.

GENERAL ABSTRACTS OF CURRENT LITERATURE

WILSON, H.: *Portal hypertension and its treatment.* Med. J. Australia, 37:2, 33-37.

Portal hypertension may be of the intrahepatic type in which case cirrhosis causes engorgement of the entire portal system. In the extra-hepatic type the cause is obstruction of the portal vein. In cases in which portal hypertension is generalized and causing hematemesis, an anastomosis between the splenic and the left renal veins gives great comfort, reduced ascites and postpones the onset of further hematemesis.

SCOTT, G. E. M.: *Celiac disease and celiac syndrome.* Med. J. Australia, 37:2, 37-46.

Scott feels that the celiac syndrome presents features indicative of a state of malnutrition, which is initiated and maintained by gastrointestinal disorders dependent on infection and toxic states. The faulty absorption of vitamins which results may play a part in the development of cystic fibrosis of the pancreas. We should regard the celiac syndrome as a physical state brought about by a number of contributing causes. At times the derangement of physiological processes in the organism may cause and maintain tissue changes which become irreversible. Scott's paper is critical and argumentative and serves to impress upon the reader the fact that the celiac syndrome today represents one of the most poorly understood conditions in pediatrics.

DOLL, R.: *Perforated carcinoma of the stomach simulating perforated gastric ulcer.* Brit. Med. J. Jan. 28, 1950, 215-218.

Of 86 perforations in men, diagnosed as being simple ulcers

at operation, seven (or 8.1 per cent) proved to be malignant within a period of three years. Eleven cases of cancer were found among 452 persons operated upon for perforation of the stomach or duodenum, and eight of the eleven were initially considered benign. This risk of cancer is an important reason for doing a partial gastrectomy as the treatment of choice in perforated gastric ulcers in men over 30 years of age.

MARSHALL, S. F.: *Surgical treatment of gallstones and their complications.* Texas State J. M. 46, 1, 12-17.

Marshall believes that cholecystectomy ought to be performed as soon as a diagnosis of gallstones has been definitely made, particularly since the mortality of gallbladder surgery has been reduced (at the Lahey Clinic) to 1.1 percent. Patients with cancer of the gallbladder show an incidence of 90 to 100 per cent of stones.

KIRKLIN, B. R.: *Advantages of the right lateral decubitus in cholecystography.* Texas State J. M. 46, 1, 5-8.

Kirklin, long since having recognized the strict requirements for satisfactory films of the gallbladder, relied for a time on the use of pitressin to rid the bowels of obscuring masses of gas. More recently he has found, however, that by placing the patient on the right side and aiming the x-ray beam laterally, through the patient, and against a vertically-held cassette, most of the obscuring shadows are eliminated because the gallbladder usually "falls away" from the bowel. By such a technique, gallstones frequently are detected in cases in which films taken in the prone position revealed none. Conversely, in some cases in which the prone film seemed to reveal stones, the lateral film indicated that the deceptive shadows did not move with the gallbladder and were indeed outside it. The prone film should always be used, and the lateral film taken when there are reasons to doubt the prone film, as for example in a case in which there is a history of colic but no stone shadow.

REIFENSTEIN, E. C. JR., DUFFY, B. J. AND GROSSMAN, M. S.: *Studies on adrenal cortical function in cancer. I. Acute effects of adrenocorticotrophic hormone in patients with gastric cancer.* Gastroenterology, 13, 6, 1949, 493-501.

Evidence is presented that patients with cancer of the stomach have adrenal cortical dysfunction. The evidence includes a failure to obtain the increases in the urinary uric acid/creatinine ratio and the urinary inorganic phosphorus/creatinine ratio which are shown by patients with non-neoplastic, non-adrenal diseases when adrenal cortex is stimulated by 25 mg. of anterior A. C. T. H.

GRAY, S. J., SCHULMAN, J. AND FALKENHEIM, M.: *The uptake of radioactive phosphorus by gastric carcinoma in the human.* Gastroenterology, 1949, 13, 6, 501-512.

Gastric cancer shows a 48.5 per cent higher turnover of radioactive phosphorus than non-cancerous gastric mucosa. Atrophic gastritis metabolizes radioactive phosphorus at the same rate as the normal mucosa. The P content of gastric cancer and the non-cancerous gastric mucosa is essentially the same.

SPARKMAN, R.: *Clinical significance of quiescent gallstones.* Texas State J. M. 46, 1, 8-11.

On the basis of statistical study, the expected mortality from cancer of the gallbladder is greater than that of prophylactic cholecystectomy applied to cases of quiescent stone in which the patient's age and physical condition is suitable for operation. Probably 10 per cent of the general public have gallstones.

BEESON, K. C.: *The soil factor in human nutritional problems.* Nutrition Reviews, Dec. 1949, 7, 12, 353-355.

Although man must increasingly learn how to utilize soils of second grade fertility, owing to the world's increasing population, a very great deal of experimental work is needed to elucidate whatever relationship exists between the soil and human nutrition. We certainly do require an abundant supply of fertilizers, but Beeson is not persuaded that organic fertilizers are any better than commercial or "chemical" fertilizers. He feels that there is even some question as to whether valid comparative experiments can be set up to measure the effects of nutritional value of plants. The soil is a dynamic system and replenishes its supply of minerals from an almost inexhaustible source, the parent rock. It appears from soil-plant studies that the composition of plant is influenced to a greater degree by the chemical composition, the microorganisms and the physical structure of the soil and by climatic factors than it is by fertilization. It is true however that fertilization can gradually improve poorer soils and maintain the better soils.

INGEGNO, ALFRED P. AND D'ALBORA, JOHN B. *Double gallbladder. Roentgenographic demonstration of a case of the "Y" type; classification of accessory gallbladder.* Am. J. Roentgenology & Rad. Th. 61, 5, 671. May 1949.

A case of true double gallbladder (vesica fellea duplex) is reported in which for the first time there was clear roentgenographic demonstration of two cystic ducts joining to form a common cystic duct. This permitted its further subclassification into the "Y" type. A classification of accessory gallbladder of clinical value is suggested and characteristics of the main types and subtypes summarized. At operation the presence of two gallbladders and two cystic ducts was verified. They were in the gallbladder fossa and had a common peritoneal investment.

Franz J. Lust.

PARSONS, B. P.: *Adenocarcinoma of the jejunum.* Am. J. Roentgen & Rad. Th. 61, 5, 680. May 1949.

Two cases of adenocarcinoma of the jejunum are reported. One was diagnosed preoperatively by roentgenological examination, the other was diagnosed on first study but on follow-up examinations the lesion could not be demonstrated. It is to be noted that a tumor large enough to cause obstruction at one examination will be completely non-demonstrable subsequently.

Franz J. Lust.

KIRSNER, JOSEPH B.; LEVIN, ERWIN, AND PALMER, WALTER LINCOLN: *Observations on the excessive nocturnal gastric secretion in patients with duodenal ulcer.* Gastroenterology 11, 5, 598. November 1948.

The output of hydrochloric acid in the nocturnal gastric secretion of five patients with recurrent or "intractable" peptic ulcer exceeded the general average for patients with duodenal ulcer. The clinical course was characterized by severe pain and by serious complications, including hemorrhage, perforation, recurrent ulcer and gastrojejunocolic fistula. The hypersecretion was not significantly reduced in the four cases so treated by large amounts of atropine or, in three instances, by enormous quantities of an enterogastrone concentrate. Roentgen irradiation of the fundus and body of the stomach effectively reduced gastric secretion in one patient, with subsequent healing of the ulcer. Irradiation diminished the output of acid temporarily in one case and no effect in two cases. Section of the vagus nerves was accompanied in two instances by a pronounced decrease in acid and by healing of the ulcer. Gastric secretion was not permanently reduced in 2 patients each of whom had undergone two vagotomies, later demonstrated to be incomplete. In one of these cases marked hypersecretion had been demonstrated despite resection of three-fourths of the stomach, including the antrum.—The important role of "intractable hypersecretion" in "intractable duodenal ulcer" is further indicated.

Franz J. Lust.

BROWN, CHARLES H., BISSONETTE, ROGER P. AND ALBEE, ROBERT D.: *Diverticula of the stomach. A report of 30 cases.* Gastroenterology 12, 1, 10. Jan. 1949.

The condition is quite rare. In 60,000 roentgenograms of the stomach, 30 cases were found. 74% of the diverticula reported in the literature and 90% of the present series were located in the cardia. Eleven or 37% of the new cases had diverticula elsewhere in the gastrointestinal tract. The most common complication of diverticulum is hemorrhage. This occurred in two of the 30 cases. There is little evidence that carcinoma develops in diverticulum of the cardia. The treatment of the patient with diverticulum of the stomach is the treatment of the associated condition.

Franz J. Lust.

CHASSIN, JAMESON L. AND HINTON, J. WILLIAM: *Primary carcinoma of the duodenal bulb mimicking duodenal ulcer.* Gastroenterology 12, 2, 312, Feb. 1949.

The authors describe three cases of carcinoma of the duodenum, which clinically and roentgenologically could not be distinguished from a benign peptic ulcer. These cases were seen within 30 months, a sign that we might assume that this condition is more frequent than generally considered.

Franz J. Lust.

ERB, WILLIAM H. AND JOHNSON, THOMAS A.: *Hyperplasia of Brunner's glands simulating duodenal polyposis.* Gastroenterology 11, 5, 740. Nov. 1948.

The roentgenological examination of a 36 year old patient re-

vealed in two instances a number of small rounded opacities in the first and second portion of the duodenum. No tenderness was elicited over the site of the lesion. The Ewald test meal showed a fasting free H Cl of 127, a total acidity of 144. The peak figures were 150/168. At operation, the mucosa of the duodenum had a cobble stone appearance which was due to hyperplasia of the Brunner's glands. Three inches of the stomach and the same amount of duodenum were removed. It is of interest that within a year the patient had a recurrence of symptoms. A marginal ulcer had developed, so that he had to be reoperated.

Franz J. Lust.

RODÉ, IVAN: *Roentgenological findings in the esophagus and stomach due to caustic poisons. (Roentgensymptome der Speiseroehren und Magenveraetzung durch aetzende Gifte).* Acta Radiol. 30, 1, 105, August 1948.

The effects of ingestion of alkaline poisons are usually more widespread in the gastro-intestinal canal than are those due to acid poisons. Usually both the esophagus and the stomach are involved. However, it may often happen that only the esophagus is affected and the stomach shows no changes. With acid poisons, the esophagus is commonly not involved and the damage is confined to the stomach. It is also more common for an isolated pyloric scar to be caused by acids than by alcalis. The pyloric scars are due to the lowered tone of the stomach and by the altered viscosity of its contents. After ingestion of an acid poison the mucosal pattern of the stomach may show a "honeycomb" appearance. The duodenum is seldom involved in the case of acid poison and the author has seen only lesions in the duodenum after alkali poisoning. It is not possible by roentgenological methods to differentiate between the scars due to acid or alkali poisoning and those due to other causes. 20 roentgenograms illustrate his interesting findings.

Franz J. Lust.

ETTINGER, ALICE: *Small intestinal pattern in sprue and similar deficiency diseases.* A. J. Roentgen. and Rad. Th. 61, 5, 658, May 1949.

This is an excellent, well illustrated report of this very important field. The author found a considerable variation in the roentgenological appearance of the small intestine of patients with deficiency syndromes. Most frequently, changes are limited to the jejunal and upper ileal loops. The lower ileal loops are not involved, while abnormalities are occasionally observed in the duodenum. In some patients delayed motility with dilatation of loops was prevalent; in others, effacing of the normal pattern (moulage sign); in still others, alternation of dilated and contracted loops. It is also worth mentioning that the abnormal pattern may only become obvious late in the examination.

It was, however, not possible to correlate the degree of roentgenological disturbance with the patient's clinical state of health. A few observations on the effect of drugs, such as prostigmine and mecholyl, upon the appearance of the small intestine of patients with sprue have been made. Two cases showed a normal response to prostigmine, which is in contrast to other observations. Following effective sprue therapy, there was a return of the roentgenological appearance towards normal in some patients, while in others the improvement of the clinical status on an efficient antisprue management was not accompanied by a corresponding improvement of intestinal pattern. Clinically, there was no correspondence in the disturbance of absorption of fat, carbohydrate and protein in a given case. The frequency of association of abdominal distention and peripheral edema has been rather striking in nearly two-thirds of the cases.

Franz J. Lust.

KEIL, P. G.: *Gastritis in the dyspeptic.* Gastroent. 1949, 13, 4, 319-321.

In 173 cases of dyspepsia having no ulcer, 24 per cent were gastroscopically found to have gastritis, while 76 per cent had normal looking mucosa. In 113 cases with duodenal ulcer, 82 per cent had normal looking mucosa and 14 per cent had gastritis. In a total of 600 consecutive gastroscopies, including the cases mentioned, gastritis was found in less than 20 percent. The usual symptoms of gastritis were distress after meals, boring epigastric pain, nausea, and burning. Patients with gastritis alone responded as well to the ulcer regime as did those with ulcer.

UTTLEY, K. F. M.: *The possible relationship between abdominal adenitis, appendicitis, tonsillitis and glandular fever.* (New Zealand Med. J., 48, 268, 540-555).

The thesis of the author might be stated in an over-simplified form as follows,—glandular fever (with a positive Paul-Bunnell test) is capable of involving most of the lymphoid tissue of the body, particularly the abdominal glands, thoracic glands and the tonsils. Since the lymphoid tissues of the appendix are capable of swelling up and occluding the lumen of the appendix, there can be little doubt that not a few cases of acute appendicitis are due to the infective agent of glandular fever. The author presents a wealth of statistical data from many sources which seem to give his theory considerable plausibility. Naturally an acutely inflamed appendix must always be removed. However, the argument might lessen the number of tonsillectomies done in cases in which the tonsils could be regarded as having merely shared the body-wide lymphoid reaction described.

LING, C. C., AND TAUR, S. S.: *A fatal case of clonorchis sinensis infestation.* Chinese Med. J. August, 1949, 67, 414-420.

A fatal case of Clonorchis infestation with postmortem findings is presented. The diagnosis was missed clinically but made by liver aspiration immediately after death, yielding more than 20 worms. Altogether the autopsy yielded more than 900 worms. The chief diagnostic clinical feature is the presence of thick irregular cords of greatly dilated bile ducts giving rise to a roughened surface of the liver. The disease which is widespread is usually not fatal, but benign. The trematode causing it was discovered in 1874 by J. F. P. McConnell.

RENNIE, J. B., LAND, F. T. AND PARK, S. D. S.: *The short esophagus (report of 31 cases).* Brit. Med. J. December 24, 1949, 1443-49.

In a period of ten years, dysphagia in 26 patients was found to be due to simple ulcer or stricture of the lower end of the gullet, associated with x-ray findings of gastric hiatal hernia and shortening of the esophagus. The diagnosis was not often considered, and proof was obtained only by x-ray with occasional esophagoscopies and biopsies. Dysphagia and ulcer pain developed during the later months of pregnancy in 5 patients, and immediately after abdominal operations in 3. In 5 patients there were no esophageal symptoms, 3 being admitted because of massive hematemesis, 1 because of anemia and the fifth gave a long history of pain and flatulence for which her gall bladder had been removed without benefit. Bright in 1836 was one of the first to notice short gullets at autopsy.

CRAVOOR, A. G.: *Psychosomatic factors in oral disease.* Bull. U. S. Army Med. Dept. 1949, IX, 12, 987-992.

A change in the chemistry of the saliva brought about by a chronic emotional tension may at times be a cause of periodontal disease. The blood supply of the mouth is important to dental health and it may be increased or decreased by vasomotor imbalance on an emotional basis. Some patients like to have teeth extracted as a means of expelling an unconscious guilt complex. The common "burning mouth" is frequently a purely nervous phenomenon. Where sexual gratification is lacking, orolingual discomfort is by no means uncommon.

VICKERS, H. R.: *Sensitization to denture material as a cause of angular stomatitis.* Brit. Med. J. Nov. 12, 1949, 1091-1092.

The author presents 3 cases in which he was able to prove that denture material was an allergen producing stomatitis, glossitis, and erecking of the angles of the mouth. He scraped denture material and used the scrapings as a patch test on the upper arm for 48 hours. In positive cases he obtained definite reactions. The condition may be helped by removing false teeth at night and cured by changing the denture material.

LINTON, R. R.: *The surgical treatment of bleeding esophageal varices by portal systemic shunts, with report of 34 cases.* Ann. Int. Med. 1949, 31, 5, 794-804.

The establishment of portal system venous shunts represents a new and encouraging chapter in the treatment of bleeding esophageal varices secondary to portal hypertension. Splenectomy and the suture type of end-to-side splenorenal anastomosis with preservation of the kidney is recommended as the best operative procedure. Observations from 4 to 34 months following satisfactory portal system venous shunts revealed a splendid cessation of bleeding from the esophagus or the g. i. tract and maintenance of normal hemoglobin levels of the blood.

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THE LINING OF THE GALL BLADDER

When inflamed, the gall bladder lining becomes thickened and coarse to a variable degree. Biliary stasis is believed to be a major factor in inciting a catarrhal inflammation which, with secondary infection, may progress to a more virulent cholecystitis with or without cholelithiasis.

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a powerful hydrocholagogue and choleretic, effects a physiologic "flushing-out" of the biliary tract by inducing a copious outflow of thin watery bile low in total solids. It is of value in chronic gall-bladder cases with or without stones (provided there is no actual obstruction) . . . in functional hepatic insufficiency, in liver poisoning by drugs or anesthetics, in cirrhosis, in chronic passive congestion of the liver. It is contra-indicated in obstructive jaundice.

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SCIENTISTS EXPERIMENTING WITH NEW CURARE-LIKE DRUG

Laboratory experimentation with the new curare-like drug to induce muscular relaxation was reported recently by Dr. James O. Hoppe, member of the staff of the Sterling-Winthrop Research Institute.

Dr. Hoppe's paper was prepared with Drs. A. E. Soria and C. J. Cavallito for presentation this morning before the American Society for Pharmacology and Experimental Therapeutics, a section of the Federation of the American Societies for Experimental Biology, meeting in Convention Hall here.

The new drug is one of a series of 40 similar compounds under test at the Institute. It is known as yet only by its laboratory number WIN 2747.

What is being sought is a synthetic curare-like drug for use in producing skeletal muscle relaxation during surgical anesthesia and in electric shock therapy. Such a drug would also have therapeutic uses wherever an abnormal increase in skeletal muscle tone is involved.

"In laboratory animals WIN 2747 has shown a high order of activity," Dr. Hoppe said. "It seems to have little or no effect on the blood pressure at curarizing dose levels, and it also appears to have little effect on the heart.

"In addition to supplying a possible new therapeutic agent, the new series of compounds show certain relationships between chemical structure, physical properties and biological activity which may give us a more intimate clue as to the site and mechanism of action of curarimimetic drugs," Dr. Hoppe concluded.

First discovery of the series about a year and a half ago was accidental. Dr. Cavallito and co-workers in the Chemistry division of the Sterling-Winthrop Research Institute have prepared several of the present series of compounds for testing as potential antibiotic substances. During the course of routine laboratory study, these were found to be relatively poor antibiotics but instead had a very high curare-like activity.

The drug, curare, a prototype of the newly synthesized compound, is an extract prepared from the crude drug *Chondodendron tomentosum*. It was originally used as an arrow poison by South American natives. A slight wound inflicted by one of these poisoned arrows was sufficient to produce a quickly fatal muscle paralysis in its victims. Although known for hundreds of years, only recently has a method been found to enable doctors to use curare effectively and safely as a medicine in the treatment of hyperactive skeletal muscle conditions.

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*PB abbreviated designation for phenobarbital.
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A. H. ROBINS COMPANY, INC. APPOINTS RESEARCH CHEMIST

Dr. Robert S. Murphey, organic chemist formerly engaged in research work at The University of Virginia for the National Cancer Institute, has joined the research staff of The A. H. Robins Company, Inc. of Richmond, Va., where he will be in charge of organic synthesis. His appointment was announced by E. Claiborne Robins, president of the rapidly expanding drug manufacturing firm, which recently added twenty-two new trainees to its national sales organization.

During his affiliation with the National Cancer Institute, Dr. Murphey worked on the synthesis of various organic compounds with tumor-necrotizing properties. He

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has specialized in amino ketones and amino alcohols of potential therapeutic value; and reports of successive studies jointly undertaken by Dr. Murphy and his co-workers have been published in the Journal of the American Chemical Society during the last two years.

A native of Littleton, N. C., but a resident of Richmond since 1929, Dr. Murphey belongs to these leading professional organizations: The American Chemical Society, The American Association of the Advancement of Science, The Society of the Sigma Xi, The Virginia Academy of Science, and Alpha Chi Sigma (national fraternity of chemists).

Dr. Murphey was graduated from the University of Richmond and holds a doctorate from The University of Virginia.

ROBITUSSIN

With its formulation based entirely on scientific observations, a new cough syrup, *Robitussin*, is being extensively promoted by A. H. Robins, Inc. of Richmond, Va.

As a product of research, Robitussin offers now a rational approach to the management of cough. As such, the firm claims Robitussin should logically supersede and replace those empirical formulations which up to the present have widely prevailed in cough remedies.

Robitussin (per 1 teaspoonful) contains: Glyceryl Guaiacolate 100 mg. Desoxyephedrine Hydrochloride 1 mg. (In a palatable aromatic syrup).

According to investigators who evaluated practically all the drugs used clinically as expectorants, glyceryl guaiacolate has the greatest antitussive-expectorant efficiency in increasing the secretion of respiratory tract fluid. Controlled experiments demonstrated that coughing decreased sharply and expectoration became much freer when glyceryl guaiacolate was administered to patients suffering with acute bronchitis, bronchitis with asthma, chronic pulmonary fibrosis, pulmonary tuberculosis, and the common cold.

Robitussin's second ingredient, desoxyephedrine hydrochloride, prevents or decreases spasm of the bronchial musculature thus minimizing it as a contributing factor to coughing. This ingredient, too, decreases psychic depression and fatigue, according to laboratory evidence.

Also, Robitussin is said to be one of the most palatable of all antitussive-expectorants.

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postmortem studies reveal 4 times greater cholesterol content of coronary arteries in fatal coronary thrombosis[1]

"The average cholesterol content of the coronary arteries in a group of patients who died from an acute coronary artery thrombosis was four times as great as the average cholesterol content of the coronary arteries in a comparable group of control patients."

"Hypercholesterolemia was found in most of the patients who died of acute coronary artery thrombosis, as compared to a normal blood cholesterol average in the comparable control group."[1]

Accumulating evidence shows that lipotropic therapy will reduce elevated blood cholesterol levels[2,3,4]... and even may "prevent or mitigate" cholesterol depositions in the intima of blood vessels in man and animals.

It has already been reported that in patients who have had acute coronary occlusion, lipotropic therapy may significantly prolong life over an untreated group with the same diagnosis.[5]

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dl-Methionine	1.0 Gm.
Inositol	0.75 Gm.
Liver fractions from	36.0 Gm. liver

*present in Methischol Syrup as 1.15 Gm. choline chloride.

supplied in bottles of 100, 250, 500 and 1000 capsules, and 16 oz. and 1 gallon syrup

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1. Morrison, L. M. and Johnson, K. D.: Amer. Heart J. 29:31, Jan. 1950.
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in peptic ulcer

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You want.....**FAST HEALING**

Creamalin relieves ulcer pain in minutes because it is truly *amorphous* aluminum hydroxide, the form emphasized by Sollmann[1] as being most soluble. Greater solubility makes Creamalin rapidly available for neutralization. Also, Creamalin is a *reactive* gel. Reactive gels exhibit greater acid-combining power.[2]

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1. Sollmann, T.: A Manual of Pharmacology. Philadelphia, W. B. Saunders Co., 7th ed., 1948, p. 938.
2. Batterman, R. C., and Ehrenfeld, L.: *Gastroenterology*, 9:141, Aug., 1947.

Creamalin®

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NEW YORK, N.Y. • WINDSOR, ONT.

The Neurogenic Approach—
in Peptic Ulcer Therapy

Banthine*

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Unlike the antacid drugs, Banthine does not effect its action within the gastrointestinal canal, but on the nervous mechanism.

Laboratory and clinical observations indicate that it acts as a true anticholinergic drug. Its effects take place at both the parasympathetic and sympathetic ganglions, and at the parasympathetic postganglionic nerve endings.

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As a result of reducing the vagotonia of ulcer patients, Banthine consistently decreases hypermotility and usually decreases hyperacidity.

Clinical experience has evidenced the rationale of this approach. Subjectively, ulcer symptoms have been relieved as soon as fifteen minutes after the first dose, with continued relief as long as the drug is continued at regular intervals. Objectively, motor and secretory inhibition has been demonstrated by intragastric balloon, analysis of gastric contents and other laboratory procedures; healing of resistant ulcers has been demonstrated roentgenographically.

TOXICITY AND PRECAUTIONS

Symptoms, such as some dryness of the mouth, mild blurring of vision, slight difficulty of urination or gastric fulness, may occur but usually disappear or decrease on continued medication; if severe, they may require dosage readjustment. Untoward reactions with Banthine therapy have not been encountered after eighteen months of clinical use.

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